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NEWS 19	May 19	Simultaneous left and right truncation added to WSCA
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 29 Jul 2003 (20030729/PD)
FILE LAST UPDATED: 29 Jul 2003 (20030729/ED)
HIGHEST GRANTED PATENT NUMBER: US6601238
HIGHEST APPLICATION PUBLICATION NUMBER: US2003140390
CA INDEXING IS CURRENT THROUGH 29 Jul 2003 (20030729/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 29 Jul 2003 (20030729/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2003

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=> S RHEUMATOID ARTHRITIS AND ACETYL AND SULFONYLAMINOCARBONYL
         19565 RHEUMATOID
         28994 ARTHRITIS
         18220 RHEUMATOID ARTHRITIS
                 (RHEUMATOID(W)ARTHRITIS)
         93753 ACETYL
           106 SULFONYLAMINOCARBONYL
L1   16 RHEUMATOID ARTHRITIS AND ACETYL AND SULFONYLAMINOCARBONYL

=> S L16 AND PD<2001
L16 NOT FOUND
The L-number entered could not be found. To see the definition of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> S L1 AND PD<2001

2778458 PD<2001
(PD<20010000)
L2 10 L1 AND PD<2001

=> D L2 1-10 BIB, AB, KWIC

L2 ANSWER 1 OF 10 USPATFULL on STN
AN 2000:9876 USPATFULL
TI Peptide, peptide analog and amino acid analog protease inhibitors
IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States
PA Sibia Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 6017887 20000125 <--
AI US 1995-443931 19950518 (8)
RLI Continuation of Ser. No. US 1995-403420, filed on 13 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995, now patented, Pat. No. US 5804560
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Lukton, David
LREP Seidman, Stephanie L.Heller Ehrman White & McAuliffe
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3617
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; R.sub.B is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.
PI US 6017887 20000125 <--
AB . . . is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; R.sub.B is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon,. . .
SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e.g., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .
SUMM Examples of suitable N-terminal blocking groups include, but are not limited to, formyl, t-butyloxycarbonyl, isopropyloxycarbonyl, allyloxycarbonyl, **acetyl**, trifluoracetyl, methyl, ethyl, benzyl, benzoyl, acetoacetyl, chloroacetyl, succinyl, phthaloxy, phenoxycarbonyl, methoxysuccinyl, p-methoxybenzenesulfonyl, p-toluenesulfonyl, isovaleroyl, methanesulfonyl, benzyloxycarbonyl, substituted benzyloxycarbonyl, adipyl, suberyl, thalamido-, morpholino-, azelayl, dansyl, tosyl, 2,4-dinitrophenyl, fluorenylmethoxycarbonyl, methoxyazelayl, methoxyadipyl, methoxysuberyl, 1-adamantanesulfonyl, 1-adamantaneacetyl, 2-carbobenzoyl, phenylacetyl, t-butylacetyl, bis[(1-methyl)methyl]**acetyl**, and thioproline.

SUMM . . . alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); and (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl, and 4-[-(4-bromophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids. . .

L2 ANSWER 2 OF 10 USPATFULL on STN
AN 1999:170588 USPATFULL
TI Perfluoroalkyl ketone inhibitors of elastase and processes for making the same
IN Curran, Timothy T., Chester, NY, United States
Burkhart, Joseph P., Plainfield, IN, United States
Angelastro, Michael R., Mason, OH, United States
Peet, Norton P., Cincinnati, OH, United States
Metz, Jr., William A., Loveland, OH, United States
PA Hoechst Marion Roussel, Inc., Bridgewater, NJ, United States (U.S. corporation)
PI US 6008196 19991228 <--
WO 9533762 19951214 <--
AI US 1996-737905 19961122 (8)
WO 1995-US5363 19950501
19961122 PCT 371 date
19961122 PCT 102(e) date
RLI Continuation of Ser. No. US 1994-327520, filed on 20 Oct 1994, now patented, Pat. No. US 5403052 which is a continuation-in-part of Ser. No. US 1994-252857, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Celsa, Bennett
LREP Gupta, Balaram
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1792
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compounds which are inhibitors of elastase, particularly human neutrophil elastase, and to novel processes for making the same. As inhibitors of human neutrophil elastase, the compounds are useful in the treatment of a patient afflicted with a neutrophil associated inflammatory disease.
PI US 6008196 19991228 <--
WO 9533762 19951214 <--
SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .
SUMM K is hydrogen, formyl, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, phenylacetyl, t-butylacetyl, bis((1-naphthyl)methyl) **acetyl**,
SUMM . . . useful as inhibitors of elastase. The compounds of formula I exhibit an anti-inflammatory effect useful in the treatment of gout, **rheumatoid arthritis** and other inflammatory diseases, such as adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, cystic fibrosis, chronic bronchitis, chronic obstructive. . .
SUMM K' is hydrogen, formyl, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl,

methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, phenylacetyl, t-butylacetyl, bis((1-naphthyl)methyl) **acetyl**, --C(.dbd.O)N--(CH.sub.3).sub.2, ##STR5## --A--R.sub.2 wherein ##STR6## R.sub.z is an aryl group containing 6, 10 or 12 carbons suitably substituted by 1. . .

SUMM . . . structure (L1) is described in J. Am. Chem. Soc., 114, 3157-59 (1992). In addition, substituted amino acids K--P.sub.4 wherein (is **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, phenylacetyl, t-butylacetyl, bis [(1-naphthyl)-methyl)**acetyl** or --A--R.sub.z wherein ##STR21## R.sub.z is an aryl group containing 6, 10 or 12 carbons suitably, suitably substituted by 1. . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

DETD . . . respiratory distress syndrome, septicemia, chronic bronchitis, inflammatory bowel disease (particularly ulcerative colitis or Crohn's disease), disseminated intravascular coagulation, gout and **rheumatoid arthritis**. Compounds of formulae (I)-(IV) which are particularly preferred for the treatment of neutrophil associated inflammatory diseases include:

DETD . . . limited to emphysema, cystic fibrosis, adult respiratory distress syndrome, chronic bronchitis, inflammatory bowel disease, septicemia, disseminated intravascular coagulation, gout and **rheumatoid arthritis**. However, it is understood that the present invention is not limited by any particular theory or proposed mechanism to explain. . .

L2 ANSWER 3 OF 10 USPATFULL on STN
AN 1999:132782 USPATFULL
TI Acylated enol derivatives as prodrugs of elastase inhibitors
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., West Chester, OH, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Merrell Pharmaceuticals Inc., Bridgewater, NJ, United States (U.S. corporation)
PI US 5972897 19991026 <--
AI US 1997-882764 19970626 (8)
RLI Division of Ser. No. US 1996-670136, filed on 25 Jun 1996, now patented, Pat. No. US 5698523, issued on 16 Dec 1997 which is a continuation of Ser. No. US 1995-420859, filed on 19 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-252798, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Stockton, Laura L.
LREP Gupta, Balaram
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1983
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of known elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema or as prodrugs of compounds which are useful in the treatment of said diseases.
PI US 5972897 19991026 <--
SUMM . . . agent contributing to the tissue destruction associated with a

number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .

SUMM K is hydrogen, formyl, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, phenylacetyl, t-butylacetyl, bis((1-naphthyl)methyl) **acetyl**, --C(O)N--(CH.sub.3).sub.2, ##STR3## --A--R.sub.z wherein ##STR4## R.sub.z is an aryl group containing 6, 10 or 12 carbons suitably substituted by 1. . .

SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.

DETD (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

DETD . . . P.sub.2, P.sub.3 and K-P.sub.4 wherein K is hydrogen are commercially available. In addition, amino protecting group K wherein K is **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxbenzoyl, phenylacetyl, t-butylacetyl, bis [(1-naphthyl)methyl]**acetyl** or --A--R.sub.z wherein ##STR15## Rz is an aryl group containing 6, 10 or 12 carbons suitably substituted by 1 to. . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

DETD Preparation of (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide ##STR46## Method A; step a: N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]-L-prolinamide (54)

DETD To a stirred light suspension of 4-[(4-chlorophenyl) **sulfonylaminocarbonyl**]benzoic acid (0.68 g, 2.02 mmol; EP Pat. Appl. Publ. No. 0189305 B1) in CH.sub.2 Cl.sub.2 (18 mL) and DMF (2. . .

DETD (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide (MDL 105,928)

DETD . . . of formula I will be particularly useful nalude: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .

DETD (E)-N-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .

CLM What is claimed is:

9. A compound of claim 1 wherein said compound is (E)-N-[4-[(4-

chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

L2 ANSWER 4 OF 10 USPATFULL on STN
AN 1999:128716 USPATFULL
TI Peptide, peptide analog and amino acid analog protease inhibitors
IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States
PA SIBIA Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 5969100 19991019 <--
AI US 1995-403420 19950313 (8)
RLI Continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995, now patented, Pat. No. US 5804560
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia; Assistant Examiner: Lukton, David
LREP Seidman, Stephanie L.Heller Ehrman White & McAuliffe
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; R.sub.B is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.
PI US 5969100 19991019 <--
AB . . . is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; R.sub.B is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon,. . .
SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e.g., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .
SUMM Examples of suitable N-terminal blocking groups include, but are not limited to, formyl, t-butyloxycarbonyl, isopropyloxycarbonyl, allyloxycarbonyl, **acetyl**, trifluoracetyl, methyl, ethyl, benzyl, benzoyl, acetoacetyl, chloroacetyl, succinyl, phthaloxy, phenoxycarbonyl, methoxysuccinyl, p-methoxybenzenesulfonyl, p-toluenesulfonyl, isovaleroyl, methanesulfonyl, benzyloxycarbonyl, substituted benzyloxycarbonyl, adipyl, suberyl, thalamido-, morpholino-, azelayl, dansyl, tosyl, 2,4-dinitrophenyl, fluorenylmethoxycarbonyl, methoxyazelayl, methoxyadipyl, methoxysuberyl, 1-adamantanesulfonyl, 1-adamantaneacetyl, 2-carbobenzoyl, phenylacetyl, t-butylacetyl, bis[(1-methyl)methyl]**acetyl**, and thioproline.
SUMM . . . (6) alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); and (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl)**sulfonylaminocarbonyl**

]phenyl carbonyl, and 4-[-(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids is. . .

L2 ANSWER 5 OF 10 USPATFULL on STN
AN 1999:106562 USPATFULL
TI Acylated enol derivatives of .alpha.-ketoesters and .alpha.-ketoamides
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., Plainfield, IN, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Hoechst Marion Roussel, Inc., Bridgewater, NJ, United States (U.S. corporation)
PI US 5948886 19990907 <--
AI US 1997-978096 19971125 (8)
RLI Continuation of Ser. No. US 1996-754081, filed on 20 Nov 1996, now abandoned
PRAI US 1996-31083P 19961201 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delacroix-Muirheid, C.
LREP Gupta, Balaram
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1641
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of .alpha.-ketoesters and .alpha.-ketoamides. The compounds of this invention are either prodrugs of known elastase inhibitors or are elastase inhibitors in their own right and are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema.
PI US 5948886 19990907 <--
SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .
SUMM . . . groups of the amino acids at the P.sub.3 and P.sub.4 positions. Moreover, elastase inhibitors containing typical N-protecting groups such as **acetyl**, succinyl, t-butyloxy-carbonyl, carbobenzyloxy, 4-((4-chlorophenyl)sulfonylamino-carbonyl)phenylcarbonyl, and the like have been specifically disclosed.
SUMM K is hydrogen, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR2## wherein Z is N or CH, B is a group of the. . .
SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.
SUMM . . . P.sub.2, P.sub.3 and K-P.sub.4 wherein K is hydrogen are commercially available. In addition, amino protecting group K wherein K is **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl,

carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, and 4-(**sulfonylaminocarbonyl**)phenylcarbonyl are described in European Patent Appl. Publ. No. 363 284, published Apr. 11, 1990 and U.S. Pat. No. 4,910,190, issued. . .

DETD Preparation of L-Prolinamide, N-[4-[[[(4-chlorohenyl)sulfonyl]amino]carbonyl]benzoyl]-L-valyl-N-[2-(acetyloxy)-3-amino-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E) ##STR25## a) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-COOH

DETD Scheme G, step a; Dissolve N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CO.sub.2 CH.sub.3 (677 mg, 1.0 mmol) in a THF:methanol:water (1:1:1) solvent mixture (30 mL) and treat with 1.0 N aqueous lithium. . .

DETD b) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CONH.sub.2

DETD Preparation of L-Prolinamide, N-[4-[[[(4-chlorophenyl)sulfonyl]amino]carbonyl]benzoyl]-L-valyl-N-[1-(1-methylethyl)-3-oxo-2-(acetyloxy)-3-(phenylamino)-1-propenyl]-, (E) ##STR26## a) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CONHC.sub.6 H.sub.5

DETD Preparation of L-Prolinamide, N-**acetyl**-L-valyl-N-[2-(acetyloxy)-3-ethoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E) ##STR27## a) Preparation of Ethyl 3-Amino-2-hydroxy-4-methyl-pentanoate.cndot.hydrochloride

DETD b) Preparation of Ethyl 3-[(N-**Acetyl**-L-valyl-L-prolyl)amino]-2-hydroxy-4-methylpentanoate

DETD c) Preparation of N-**Acetyl**-L-valyl-N-[3-ethoxy-1-(1-methylethyl)-2,3-dioxopropyl]-L-prolinamide

DETD d) Preparation of L-Prolinamide, N-**acetyl**-L-valyl-N-[2-(acetyloxy)-3-ethoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E)

DETD Preparation of L-Prolinamide, N-**acetyl**-L-prolyl-L-valyl-N-[2-(acetyloxy)-3-methoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E)- (SEQ. ID NO. 7) ##STR28##

DETD Scheme A; Treat N-**Acetyl**-L-prolyl-L-alanyl-N-(3-methoxy-1-methyl-2,3-dioxopropyl)-L-prolinamide (88 mg, 0.20 mmol)(Peet, N. P. et al., J. Med. Chem., 33, 394 (1990)) with acetic anhydride (0.19 mL, 2.0. . .

DETD . . . pyridinyl or tetrahydroquinoline, preferably Pro; P.sub.3 is Ile, Val or Ala; P.sub.4 is Ala or is deleted and K is **acetyl**, t-butyloxycarbonyl, succinyl, methyoxysuccinyl, 4-((chlorophenyl)sulfonylamino-carbonyl)-phenylcarbonyl, or is a group of the formula ##STR40## wherein Z is N or CH, B is. . .

DETD L-Prolinamide, N-**acetyl**-L-valyl-N-[2-(acetyloxy)-3-ethoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E) -;

DETD L-Prolinamide, N-**acetyl**-L-valyl-N-[2-(acetyloxy)-3-ethoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (Z)-;

DETD L-Prolinamide, N-**acetyl**-L-lysyl-N-[2-(acetyloxy)-3-ethoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E)-;

DETD L-Prolinamide, N-**acetyl**-L-prolyl-L-valyl-N-[2-(acetyloxy)-3-methoxy-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E)-; (SEQ. ID NO. 7)

DETD . . . of formula I will be particularly useful include: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .

DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and

inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .

CLM What is claimed:

. . . Ile, Nle, Val, Nva, or Lys P.sub.4 is Ala, bAla, Val, Nva, bVal, Pro or is deleted; K is hydrogen, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR43## wherein Z is N or CH, B is a group of the. . .

. . . Pro, Aze or Tic; P.sub.3 is Ile, Val, or Ala; P.sub.4 is Ala, Pro or is deleted; and K is **acetyl**, succinyl, t-butyloxycarbonyl, carbobenzyloxy, methoxysuccinyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formula ##STR45## wherein Z is N or CH, B is a group of the. . .

3. A compound of claim 2 wherein R.sub.1 is isopropyl; P.sub.2 is Pro; and K is **acetyl**, t-butyloxycarbonyl, succinyl, methyoxysuccinyl, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, or is a group of the formula ##STR47## wherein Z is N or CH, B is a group of the. . .

L2 ANSWER 6 OF 10 USPATFULL on STN

AN 1999:22082 USPATFULL

TI Methods of treating neurodegenerative disorders using protease inhibitors

IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States

PA Sibia Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)

PI US 5872101 19990216 <--

AI US 1995-444361 19950518 (8)

RLI Continuation of Ser. No. US 1995-403420, filed on 13 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995

DT Utility

FS Granted

EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Lukton, David

LREP Stephanie L. Seidman Heller Ehrman White & McAuliffe

CLMN Number of Claims: 31

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 3945

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; R.sub.8 is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.

PI US 5872101 19990216 <--

AB . . . is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably

benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; R.sub.8 is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon,. . .

SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e.g., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .

SUMM Examples of suitable N-terminal blocking groups include, but are not limited to, formyl, t-butyloxycarbonyl, isopropyloxycarbonyl, allyloxycarbonyl, **acetyl**, trifluoracetyl, methyl, ethyl, benzyl, benzoyl, acetoacetyl, chloroacetyl, succinyl, phthaloxy, phenoxycarbonyl, methoxysuccinyl, p-methoxybenzenesulfonyl, p-toluenesulfonyl, isovaleroyl, methanesulfonyl, benzyloxycarbonyl, substituted benzyloxycarbonyl, adipyl, suberyl, thalamido-, morpholino-, azelayl, dansyl, tosyl, 2,4-dinitrophenyl, fluorenylmethoxycarbonyl, methoxyazelayl, methoxyadipyl, methoxysuberyl, 1-adamantanesulfonyl, 1-adamantaneacetyl, 2-carbobenzoyl, phenylacetyl, t-butylacetyl, bis[(1-methyl)methyl]**acetyl**, and thioproline.

SUMM . . . (6) alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl, and 4-[-(4-bromophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids. . .

CLM What is claimed is:

. . . ethyl; R.sub.3 is iso-butyl, benzyl or phenyl; R.sub.5 is C.sub.1-4 alkyl; R.sub.6 is H or C.sub.1-4 alkyl; R.sub.7 --(Q).sub.n is **acetyl** or benzyloxycarbonyl (Cbz); Q is --C(O)-- or --O--C(O)--; R.sub.B is C.sub.1-4 alkyl or C.sub.2-4 alkenyl; R.sub.A is --(T).sub.m --(D).sub.m --R.sub.1,. . .

. . . iso-butyl; R.sub.5 is C.sub.1-4 alkyl; R.sub.6 is H or C.sub.1-4 alkyl; R.sub.7 --(Q).sub.n is selected from the group consisting of **acetyl**, benzyloxycarbonyl (Cbz), 9-fluorenylmethylcarbonate (Fmoc), BOC and tosyl; Q is --C(O)--, --S(O).sub.2 -- or --O--C(O)--; R.sub.B is C.sub.1-4 alkyl or C.sub.2-4. . .

. . . ethyl; R.sub.3 is iso-butyl, benzyl or phenyl; R.sub.5 is C.sub.1-4 alkyl; R.sub.6 is H or C.sub.1-4 alkyl; R.sub.7 --(Q).sub.n is **acetyl** or benzyloxycarbonyl (Cbz); Q is --C(O)-- or --O--C(O)--; R.sub.B is C.sub.1-4 alkyl or C.sub.2-4 alkenyl; R.sub.A is --(T).sub.m --(D).sub.m --R.sub.1,. . .

L2 ANSWER 7 OF 10 USPATFULL on STN
AN 1999:12911 USPATFULL
TI Methods of treating neurodegenerative disorders using protease inhibitors
IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States
PA Sibia Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 5863902 19990126 <--
AI US 1995-444912 19950518 (8)
RLI Continuation of Ser. No. US 1995-403420, filed on 13 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Lukton, David
LREP Seidman, Stephanie L.Heller Erhman White & McAuliffe
CLMN Number of Claims: 19
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 3888
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 -(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; RB is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.
PI US 5863902 19990126 <--
AB . . . is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 -(Q).sub.n is preferably benzyloxycarbonyl or **acetyl**; Q is preferably --C(O)--; RB is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon,. . .
SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .
SUMM Examples of suitable N-terminal blocking groups include, but are not limited to, formyl, t-butyloxycarbonyl, isopropyloxycarbonyl, allyloxycarbonyl, **acetyl**, triflgoracetyl, methyl, ethyl, benzyl, benzoyl, acetoacetyl, chloroacetyl, succinyl, phthaloxy, phenoxycarbonyl, methoxysuccinyl, p-methoxybenzenesulfonyl, p-toluenesulfonyl, isovaleroyl, methanesulfonyl, benzyfoxycarbonyl, substituted benzyloxycarbonyl, adipyl, suberyl, thalamido-, morpholino-, azelayl, dansyl, tosyl, 2,4-dinitrophenyl, fluorenyl-methoxycarbonyl, methoxyazelayl, methoxyadipyl, methoxysuberyl, 1-ada-mantanesulfonyl, 1-adamantaneacetyl, 2-carbobenzoyl, phenylacetyl, t-butylacetyl, bis[(1-methyl)methyl]**acetyl**, and thioproline.
SUMM . . . alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); and (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl, and 4-[-(4-bromophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids. . .

L2 ANSWER 8 OF 10 USPATFULL on STN
AN 97:118015 USPATFULL
TI Acylated enol derivatives as prodrugs of elastase inhibitors
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., West Chester, OH, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Merrell Pharmaceuticals Inc., Cincinnati, OH, United States (U.S. corporation)
PI US 5698523 19971216 <--
AI US 1996-670136 19960625 (8)
RLI Continuation of Ser. No. US 1995-420859, filed on 19 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-252798, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Stockton, Laura L.
LREP Boudreaux, William R.

CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of known elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema or as prodrugs of compounds which are useful in the treatment of said diseases.
PI US 5698523 19971216 <--
SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .
SUMM K is hydrogen, formyl, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, phenylacetyl, t-butylacetyl, bis((1-naphthyl)methyl) **acetyl**, --C(O)N--(CH.sub.3).sub.2, ##STR2## -A-R.sub.z wherein ##STR3## R.sub.z is an aryl group containing 6, 10 or 12 carbons suitably substituted by 1. . .
SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.
DETD (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.
DETD . . . P.sub.2, P.sub.3 and K-P.sub.4 wherein K is hydrogen are commercially available. In addition, amino protecting group K wherein K is **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxbenzoyl, phenylacetyl, t-butylacetyl, bis [(1-naphthyl)methyl]**acetyl** or -A-R.sub.z wherein A is ##STR13## and Rz is an aryl group containing 6, 10 or 12 carbons suitably substituted. . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
DETD Preparation of (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide ##STR45##
DETD Method A; step a: N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]-L-prolinamide (54)
DETD To a stirred light suspension of 4-[(4-chlorophenyl) **sulfonylaminocarbonyl**]benzoic acid (0.68 g, 2.02 mmol; EP Pat. Appl. Publ. No. 0189305 B1) in CH.sub.2 Cl.sub.2 (18 mL) and DMF (2. . .
DETD Step b: (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide (MDL 105,928)
DETD . . . of formula I will be particularly useful include: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease.

Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .

DETD (E)-N-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .

CLM What is claimed:

. . . morpholino-B-group or Orn substituted on its delta amino group with a morpholino-B-group; P.sub.4 is a bond; K is hydrogen, formyl, **acetyl**, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, tosyl, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, phenylacetyl, t-butylacetyl, bis((1-naphthyl)methyl)**acetyl**, --C(O)N--(CH.sub.3).sub.2, or -A-R.sub.z wherein ##STR48## R.sub.z is an aryl group containing 6, 10 or 12 carbons substituted by 1 to. . .

L2 ANSWER 9 OF 10 USPATFULL on STN

AN 93:63173 USPATFULL

TI Tetrahydroisoquinoline amides

IN Skiles, Jerry W., Brookfield, CT, United States

PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)

PI US 5232928 19930803 <--

AI US 1991-792130 19911114 (7)

RLI Continuation of Ser. No. US 1990-536912, filed on 12 Jun 1990, now abandoned which is a continuation of Ser. No. US 1989-385140, filed on 25 Jul 1989, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Turnipseed, James H.

LREP Frankhouser, D. E., Stempel, A. R., Timbers, M-E. M.

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 769

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Tetrahydroisoquinoline amides having the general structure ##STR1## are disclosed, the substituents defined hereinbelow, which amides are useful in inhibiting human leukocyte and neutrophil elastaes.

PI US 5232928 19930803 <--

DETD . . . the treatment of tissue degenerative diseases. Additionally, such inhibitors could be used in the diagnosis and treatment of pulmonary emphysema, **rheumatoid arthritis**, osteoarthritis, and arteriosclerosis, among other diseases. The substituted amides of the present invention may be represented by the following formulae:. . .

DETD . . . lower alkyl (1-6 carbons) lower alkoxy, lower aryloxy, alkylthio, halogen, nitro, cyano, amino, aminoalkyl, aminoalkanoyl, mercapto, thioalkyl, carboxy, hydroxy, alkoxycarbonyl, **acetyl**, formyl, alkanoyl, alkanoyloxy, alkylamino, or two adjacent Z groups taken together may form a methylenedioxy ring or a dioxalane ring.

DETD A.sub.1 and A.sub.2 are hydrogen, lower alkyl, halogen, **acetyl**, or trifluoroacetyl, alkoxy, nitro, carboxy, cyano, and alkoxycarbonyl;

DETD . . . of the present invention would be useful in the diagnosis and treatment of tissue degenerative diseases such as pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress

syndrome - otherosclerosis, osteo arthritis, chronic obstructive lung disease, glomerular nephritis, inter alia.

DETD . . . be administered for the alleviation of conditions which include tissue degenerative diseases such as: pulmonary emphysema, artherosclerosis and osteo- and **rheumatoid arthritis** , in particular emphysema, and other diseases. The mode of administration may be parenteral, including the subcutaneous deposit of an osmotic. . .

DETD N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl-L-valyl]-(6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3'-(R,S)-[2'-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-leucyl]-spiro[cyclopentane-1,1'-(6.7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]]-carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-3-methyl -1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)]

DETD N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-carboxyl-pentyl)]

DETD N-[3'-(R,S)-[2'-[(2-methoxysuccinyl)amino-.alpha.-(methoxycarboxy)-4-thiazole-**acetyl**)-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)]

DETD 1,1-Dimethylethyl-4-](4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoate

DETD . . . over MgSO.sub.4 followed by filtration and evaporation a solid was obtaind which was treated with ether and filtered to yield 1,1-dimethylethyl-4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate (5.8 g, 42.3%) as a white solid (mp: above 300.degree. C.) which was used for hydrolysis.

DETD 4-](4-Chlorophenyl)**sulfonylaminocarbonyl**]benzene carboxylic acid

DETD . . . before being filtered, washed with water and dried to yield a white solid. Recrystallization from ethanol/water (1:1) gave the product 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**] benzene carboxylic acid in 63% yield melting at 285.degree.-287.degree. C.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]1,2,3,4-tetrahydro-3-isoquinolinecarboxamide

DETD . . . stated order in dry THF (35 mL) at 0.degree.-5.degree. C. L-Valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide (0.52 g, 1.21 mmol), HOBT (0.15 g, 1.1 mmol), 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzene carboxylic acid (0.37 g, 1.1 mmol), and WSCDI (0.45 g, 1.21 mmol). The mixture was stirred at 0.degree.-5.degree. C. for. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-1,2,3,4-tetrahydro-3-isoquinoline-carboxamide.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide (0.33 g, 0.44 mmol) was added to

CH.sub.2 Cl.sub.2 (15mL) followed by Dess-Martin periodinane (0.56 g, 1.3 mmol) in CH.sub.2. . .

CLM What is claimed is:

3. A compound selected from the group consisting of: N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy -1,2,3,4-tetrahydro-isoquinolyl)carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl-L-valyl]-(6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-[2-[2-Amino-.alpha.-(methoxyimino)-4-thiazoleacetyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-[2-[2-Amino-.alpha.-(carboxymethoxyimino)-4-thiazolacetyl-L-valyl]-(5,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy -1,1-dimethyl-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3'-(R,S)-[2'-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-leucyl]-spiro [cyclopentane-1,1'-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]-carbonyl]-N-[3(1,1,1-trifluoro -4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-leucyl]-(1-benzyl -5,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinolyl)]-carbonyl]-N-(3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3'-(R,S)-[2'-[2-Amino-.alpha.-(methoxyimino)-4-thiazolacetyl-L-valyl]-spiro[cyclohexane -1,1'-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl -2-oxopentyl)]amine N-[3'-(R,S)-[2'-[2-(methoxysuccinyl)amino-.alpha.-(methoxyimino)-4-thiazolacetyl-L-valyl(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-3-methyl -1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy -1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)] N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,-difluoro-2-oxo-4-methyl-1-carboxyl-pentyl)] N-[3'-(R,S)-[2'-[(2-methoxysuccinyl)amino-.alpha.-(methoxycarboxy)-4-thiazole-**acetyl**)-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)] N-[.alpha.-(methoxyimino)-2-furylacetyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

L2 ANSWER 10 OF 10 USPATFULL on STN
AN 93:50536 USPATFULL
TI N-substituted amides
IN Skiles, Jerry W., Brookfield, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 5221665 19930622 <--
AI US 1991-686918 19910416 (7)
RLI Continuation of Ser. No. US 1989-426069, filed on 27 Oct 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Lester L.

LREP Frankhouser, D. E., Stempel, A. R., Timbers, M-E. M.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB N-substituted amides which inhibit hydrolysis of elastin, are described, which compounds are tri-and di- fluoromethyl ketone amide and non-naturally occurring n-substituted amino acids derivatives.
PI US 5221665 19930622 <--
DETD . . . compounds may serve as diagnostic aids. Accordingly, such inhibitors could be used in the diagnosis and treatment of pulmonary emphysema, **rheumatoid arthritis**, osteoarthritis, and arteriosclerosis, among other diseases.
DETD . . . is preferably selected from one of the following: ##STR3## wherein A.sub.1 and A.sub.2 are each independently hydrogen, lower alkyl, halogen, **acetyl**, trihaloacetyl, trihalomethyl, alkoxy, nitro, carboxy, alkoxycarbonyl, cyano, sulfonamido, amino alkylamino, dialkylamino, carbonyl, or alkanoyl.
DETD . . . twenty-five carbon atoms and may carry substituents such as lower alkyl, alkenyl, alkynyl, hydroxy, thio, amino, alkoxy, alkylthio, alkyl-amino, halogen, **acetyl**, trifluoroacetyl, and nitro. Examples of such X-substituents include such radicals as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, norbornyl, adamantyl, phenyl, tolyl,. . .
DETD . . . of the present invention would be useful in the diagnosis and treatment of tissue degenerative diseases such as pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome, otherosclerosis, osteo arthritis, chronic obstructive lung disease, glomerular nephritis, inter alia.
DETD . . . be administered for the alleviation of conditions which include tissue degenerative diseases such as: pulmonary emphysema, arteriosclerosis and osteo- and **rheumatoid arthritis** , especially emphysema. The mode of administration may be parenteral, oral, intravenous, as a powder or liquid aerosol, or subcutaneous by. . .
DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(n-hexyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(phenyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(4-trifluoromethylphenyl)glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(3,4-dimethoxyphenyl)glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-(N-methyl) valyl-N-(2,3-dihydro-1H-inden-1-yl) glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[2-(3-indolyl)ethyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-(N-cyclopentyl)valyl-N-(benzimidazo-2-yl) glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide
DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[(N-ethoxycarbonyl)piperidin-4-yl)]glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide [2-Amino-.alpha.-(methoxyimino)-4-thiazoleacetyl]-L-valyl-N-(2, 3-dihydro-1H-inden-5-yl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[1-[2-(morpholin-4-yl)]ethyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-leucyl-N-[1-[2-(pyrid-2-yl)]ethyl]-L-alanyl-N-[3-(1, 1,1-trifluoro-4-m ethyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(2-indanylmethyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(piperidin-1-yl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[1-[3-(pyrrolidin-2-one)-1-yl]propyl] glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Phenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl-L-valyl-N-[(tetrahydro-2H-pyran-2-yl)methyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-leucyl-N-(quinuclidin-3-yl)glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[(cyclohexyl)methyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[(2-pyrrole)methyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(5,6-dimethoxy-2,3-dihydro-1H-inden-2-yl) glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[L-2-oxohexamethyleneimine-3-yl)]glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(6,7,8,9-tetrahydro-5H-benzocyclohepten-7-yl) glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(5H-benzoimidazol-6-yl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(2,3-dihydro-1H-inden-2-yl)glycyl-N-[3-(1,1,1-trifluoro-4-(3,4-methylenedioxy) phenyl-2-oxobutyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl)]-L-valyl-N-(3-carboxypropyl)glycyl-N-[3-(1, 1,1-trifluoro-4-(3,4,5-trimethoxy)phenyl-2-oxobutyl)]amide

DETD 1,1-Dimethylethyl-4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**] benzoate

DETD . . . over MgSO.sub.4 followed by filtration and evaporation a solid was obtained which was treated with ether and filtered to yield 1,1-dimethylethyl-4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate (5.8 g, 42.3%) as a white solid (mp: above 300.degree. C.) which was used for hydrolysis. 4-[(4-Chlorophenyl) **sulfonylaminocarbonyl** benzene carboxylic acid

DETD . . . before being filtered, washed with water and dried to yield a white solid. Recrystallization from ethanol/water (1:1) gave the product 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**] benzene carboxylic acid in 63% yield melting at 285.degree.-287.degree. C.

DETD [4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-Valyl-N-2-(3,4-dimethoxy)phenethyl]-glycyl-N-3-(1, 1,1-trifluoro-4-methyl-2-hydroxypentyl)] amide

DETD . . . in dry THF (35 mL) at 0.degree.-5.degree. C.: L-Valyl-N-[2-(3,4-dimethoxy)phenethyl]glycyl-N-[3-(1,

1,1-trifluoro-4-methyl-2-hydroxypentyl]amide (0.8 g, 1.63 mmol), hydroxybenzotriazole (HOBT), 0.2 g, 1.48 mmol), 4-[(4-chlorophenyl)-**sulfonylaminocarbonyl**]benzene carboxylic acid (0.5 g, 1.48 mmol), WSCDI (0.312 g, 1.63 mmol) and triethylamine (0.165 g, 1.63 mmol). The mixture was. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-Valyl-N-[2-(3,4-dimethoxy)phenethyl] glycyl-N-[3-(1,1,1-trifluoro-4-methyl- 2-hydroxypentyl)] amide (0.4 g, 0.492 mmol) was added to THF (20 mL) followed by Dess-Martin periodinane (0.42 g,. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl 1-L-Valyl-N-(2-indanyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]amide

DETD . . . following reactants were mixed in the stated order in L-valyl-N-(2-indanyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]amide (1.3 g, 2.93 mmol), hydroxybenzotriazole (HOBT), (0.36 g, 2.66 mmol), 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzene carboxylic acid (0.9 g, 2.64 mmol) and WSCDI (0.56 g, 2.92 mmol). The mixture was stirred at 0.degree.-5.degree. C. for. . .

DETD [4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-valyl-N-(2-indanyl)glycyl-N-3-(1,1,1-trifluoro-4-methyl-2-oxypentyl)lamide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(2-indanyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]amide (1.6 g, 2.1 mmol) was added to THF (25 mL) followed by Dess-Martin periodinane (2.66 g, 6.3 mmol). . .

DETD [4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl -L-Valyl-N-(exo-bicyclo2. 2.1]hept-2-yl) glycyl-N-3-(1,1,1-trifluoro-4-methyl-2-hydroxy-pentyl)]amide.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-Valyl-N-(exo-bicyclo[2,2,1]hept-2-yl)-glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxypentyl)] amide.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(exo-bicyclo[2.2.1]hept-2-yl)-glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-hydroxy-pentyl)]amide (0.6 g, 0.807 mmol) was added to CH.sub.2 Cl.sub.2 (20 mL) followed by Dess-Martin periodinane (0.69 g,. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-Valyl-N-(cyclopentyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)amide]

DETD (4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-Valyl-N-cyclopentyl-glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxypentyl)lamide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-Valyl-N-(cyclopentyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxy pentyl)]amide (0.72 g, 1.0 mmol) was added to THF (20 mL) followed by Dess-Martin periodinane (1.27 g, 3.0 mmol). . .

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* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

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=> file uspatfull
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 29 Jul 2003 (20030729/PD)
FILE LAST UPDATED: 29 Jul 2003 (20030729/ED)
HIGHEST GRANTED PATENT NUMBER: US6601238
HIGHEST APPLICATION PUBLICATION NUMBER: US2003140390
CA INDEXING IS CURRENT THROUGH 29 Jul 2003 (20030729/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 29 Jul 2003 (20030729/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2003

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>>> publications, starting in 2001, for the inventions covered in <<<
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>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
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>>> /PK, etc. <<<

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>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s rheumatoid arthritis
         19565 RHEUMATOID
         28994 ARTHRITIS
L1   18220 RHEUMATOID ARTHRITIS
                (RHEUMATOID(W)ARTHRITIS)

=> s l1 and sulfonylamino?
          2484 SULFONYLAMINO?
L2   371 L1 AND SULFONYLAMINO?

=> s l2 and carbonyl
         86711 CARBONYL
L3   285 L2 AND CARBONYL

=> s l3 and PD<1999

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       2435652 PD<1999
                 (PD<19990000)
L4           64 L3 AND PD<1999

=> s s rheumatoid arthritis and sulfonylamino and 514/602/ccls
'CCLS' IS NOT A VALID FIELD CODE
       2433700 S
         19565 RHEUMATOID
         28994 ARTHRITIS
             9 S RHEUMATOID ARTHRITIS
                 (S(W)RHEUMATOID(W)ARTHRITIS)
          2186 SULFONYLAMINO
             0 514/602/CCLS
L5           0 S RHEUMATOID ARTHRITIS AND SULFONYLAMINO AND 514/602/CCLS

=> d l4 1-64 bib, ab

L4   ANSWER 1 OF 64  USPATFULL on STN
AN     2002:346969  USPATFULL
TI     Methods and compositions useful for inhibition of angiogenesis
IN     Brooks, Peter C., Hollywood, CA, United States
       Cheresh, David A., Encinitas, CA, United States
       Silletti, Steven A., San Diego, CA, United States
PA     The Scripps Research Institute, La Jolla, CA, United States (U.S.
       corporation)
PI     US 6500924          B1   20021231
       WO 9745137  19971204                                          <--
AI     US 1999-194468           19990323 (9)
       WO 1997-US9158           19970530
PRAI   US 1996-18773P       19960531 (60)
       US 1996-15869P       19960531 (60)
DT     Utility
FS     GRANTED
EXNAM  Primary Examiner: Caputa, Anthony C.; Assistant Examiner: Nickol, Gary
       B.
LREP   Holmes, Emily, Fitting, Thomas
CLMN   Number of Claims: 6
ECL    Exemplary Claim: 1
DRWN   106 Drawing Figure(s); 46 Drawing Page(s)
LN.CNT 4939
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The present invention describes methods for inhibition of angiogenesis
       in tissues using vitronectin .alpha..sub.v.beta..sub.3 antagonists, and
       particularly for inhibiting angiogenesis in inflamed tissues and in
       tumor tissues and metastases using therapeutic compositions containing
       .alpha..sub.v.beta..sub.3 antagonists.

L4   ANSWER 2 OF 64  USPATFULL on STN
AN     2002:290938  USPATFULL
TI     N-hydroxy 4-sulfonyl butanamide compounds
IN     Villamil, Clara I., Glenview, IL, United States
       Freskos, John N., Clayton, MO, United States
       Mischke, Brent V., Defiance, MO, United States
       Mullins, Patrick B., St. Louis, MO, United States
       Heintz, Robert M., Ballwin, MO, United States
       Getman, Daniel P., Chesterfield, MO, United States
       McDonald, Joseph J., Ballwin, MO, United States
       DeCrescenzo, Gary A., St. Charles, MO, United States
       Barta, Thomas E., Evanston, IL, United States
       Becker, Daniel P., Glenview, IL, United States
PA     Monsanto Company, St. Louis, MO, United States (U.S. corporation)
PI     US 6476027          B1   20021105
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WO 9839316 19980911 <--
AI US 1999-254531 19991206 (9)
WO 1998-US4297 19980304
19991206 PCT 371 date
PRAI US 1997-35182P 19970304 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.
LREP Harness, Dickey & Pierce, P.L.C.
CLMN Number of Claims: 47
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3634
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An N-hydroxy sulfonyl butanamide compound that inter alia inhibits matrix metalloprotease activity is disclosed as are a treatment process that comprises administering a contemplated N-hydroxy sulfonyl butanamide compound in a MMP enzyme-inhibiting effective amount to a host having a condition associated with pathological matrix metalloprotease activity.

L4 ANSWER 3 OF 64 USPATFULL on STN
AN 2002:14026 USPATFULL
TI Use of matrix metalloproteinase inhibitors for treating neurological disorders and promoting wound healing
IN Bocan, Thomas Michael Andrew, Ann Arbor, MI, United States
Boxer, Peter Alan, Ann Arbor, MI, United States
Peterson, Jr., Joseph Thomas, Brighton, MI, United States
Schrier, Denis, Ann Arbor, MI, United States
White, Andrew David, Pinckney, MI, United States
PA Warner-Lambert Company, Morris Plains, NJ, United States (U.S. corporation)
PI US 6340709 B1 20020122
WO 9826773 19980625 <--
AI US 1999-269123 19990319 (9)
WO 1997-US21532 19971121
19990319 PCT 371 date
PRAI US 1996-32753P 19961217 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Fay, Zohreh
LREP Ashbrook, Charles W., Kurlandsky, David R.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3726
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a method for treating and preventing neurological disorder such as Alzheimer's disease, and for promoting wound healing comprising administering a compound characterized as being a matrix metalloproteinase inhibitor.

L4 ANSWER 4 OF 64 USPATFULL on STN
AN 2001:235249 USPATFULL
TI Piperazine compounds as inhibitors of MMP or TNF
IN Neya, Masahiro, Tsuchiura, Japan
Yamazaki, Hitoshi, Tsukuba, Japan
Kayakiri, Natsuko, Suita, Japan
Sato, Kentaro, Tsukuba, Japan
Oku, Teruo, Takatsuki, Japan
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6333324 B1 20011225

WO 9827069 19980625 <--
AI US 1999-319928 19990726 (9)
WO 1997-JP4613 19971215
19990726 PCT 371 date
19990726 PCT 102(e) date
PRAI AU 1996-4249 19961217
AU 1997-7156 19970603
AU 1997-8568 19970814
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Liu, Hong
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5901
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of formula (I) wherein A is a sulfonyl or a **carbonyl** ; R.sup.1 is an optionally substituted aryl, an optionally substituted heterocyclic group, an optionally substituted lower alkyl or an optionally substituted lower alkenyl; R.sup.2 is a hydrogen, an optionally substituted lower alkyl, an optionally substituted aryl or an optionally substituted heterocyclic group; R.sup.3 is an optionally substituted lower alkyl, an optionally substituted lower alkoxy, an optionally substituted aryloxy, an optionally substitued lower alkenyl, an optionally substituted aryl, an optionally substituted heterocyclic group or an optionally substitued amino; R.sup.4 is a hydrogen, an optionally substituted lower alkyl, an optionally substituted aryl or an optionally substituted heterocyclic group; R.sup.5 is a hydrogen, an optionally substituted lower alkyl, an optionally substituted aryl or an optionally substituted heterocyclic group; and R.sup.10 is a hydroxy or a protected hydroxy, and a pharmaceutically acceptable salt thereof. The compound of the present invention is useful as a medicament for prophylactic and therapeutic treatment of MMP- or TNF.alpha.-mediated diseases. ##STR1##

L4 ANSWER 5 OF 64 USPATFULL on STN
AN 2001:112378 USPATFULL
TI IL-8 receptor antagonists
IN Widdowson, Katherine Louisa, King of Prussia, PA, United States
Veber, Daniel Frank, Ambler, PA, United States
Jurewicz, Anthony Joseph, Royersford, PA, United States
Hertzberg, Robert Philip, Downingtown, PA, United States
Rutledge, Jr., Melvin Clarence, Lansdale, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6262113 B1 20010717
WO 9729743 19970821 <--
AI US 1998-125279 19980814 (9)
WO 1996-US13632 19960821
19980814 PCT 371 date
19980814 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1996-641990, filed on 20 Mar 1996, now patented, Pat. No. US 5886044
DT Utility
FS GRANTED
EXNAM Primary Examiner: Higel, Floyd D.; Assistant Examiner: Sackey, Ebenezer
LREP Simon, Soma G., Dinner, Dara L., Kinzig, Charles M.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5598

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel compounds and a novel use of phenyl ureas in the treatment of disease states mediated by the chemokine Interleukin-8 (IL-8).

L4 ANSWER 6 OF 64 USPATFULL on STN
AN 2001:14498 USPATFULL
TI Aryl and heteroaryl substituted fused pyrrole antiinflammatory agents
IN Zablocki, Jeffery A., Mountain View, CA, United States
Tarlton, Jr., Eugene, Superior, CO, United States
Rizzi, James P., Niwot, CO, United States
Mantlo, Nathan B., Lafayette, CO, United States
PA Amgen Inc., Thousand Oaks, CA, United States (U.S. corporation)
PI US 6180643 B1 20010130
WO 9822457 19980528 <--
AI US 1999-269600 19990608 (9)
WO 1997-US21344 19971118
19990608 PCT 371 date
19990608 PCT 102(e) date
PRAI US 1996-31207P 19961119 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Patel, Sudhaker B.
LREP Ungemach, Frank, Odre, Steven M.
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5726
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention comprises a new class of novel aryl and heteroaryl substituted fused pyrrole compounds useful for the prophylaxis and treatment of diseases or conditions, such as TNF-.alpha., IL-1.beta., IL-6 and/or IL-8 mediated diseases, and other maladies, such as pain and diabetes. In particular, the compounds of the invention are useful for the prophylaxis and treatment of diseases or conditions involving inflammation. Accordingly, the invention also comprises pharmaceutical compositions comprising the compounds of the invention, methods for the prophylaxis and treatment of inflammation and other maladies, such as pain and diabetes, using the compounds and compositions of the invention, and intermediates and processes useful for the preparation of compounds of the invention. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

L4 ANSWER 7 OF 64 USPATFULL on STN
AN 2000:161153 USPATFULL
TI Metalloproteinase inhibitors and intermediates useful for their preparation
IN Zook, Scott E., Del Mar, CA, United States
Dagnino, Jr., Raymond, San Diego, CA, United States
Deason, Michael E., Poway, CA, United States
Bender, Steven L., Oceanside, CA, United States
Melnick, Michael J., San Diego, CA, United States
PA Agouron Pharmaceuticals, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 6153757 20001128
WO 9720824 19970612 <--
AI US 1998-11971 19980629 (9)
WO 1996-US19328 19961205
19980629 PCT 371 date
19980629 PCT 102(e) date

RLI Continuation-in-part of Ser. No. US 1996-759713, filed on 6 Dec 1996, now patented, Pat. No. US 5753653
PRAI US 1995-41496P 19951208 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3755
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to compounds of formula (1) ##STR1## wherein: Z is O or S; V is a divalent radical which together with C* and N forms a ring having six ring atoms, where each of said ring atoms other than C* and N independently is unsubstituted or substituted by a suitable substituent, and at least one of said other ring atoms is a heteroatom selected from O, N and S, and the remainder is carbon atoms; and Ar is an aryl or heteroaryl group; and pharmaceutically acceptable prodrugs, salts and solvates thereof. The invention further relates to pharmaceutically acceptable prodrugs, salts and solvates of these compounds. The invention also relates to methods of inhibiting the activity of metalloproteinases by administering a compound of formula (1) or a prodrug, salt or solvate thereof. The invention further relates to pharmaceutical compositions comprising an effective amount of these compounds, prodrugs, salts, and solvates. The invention still further relates to methods and intermediates useful for preparing these compounds, prodrugs, salts, and solvates.

L4 ANSWER 8 OF 64 USPATFULL on STN
AN 2000:113960 USPATFULL
TI Amino acid derivatives and their use as phospholipase A.sub.2 inhibitor
IN Takase, Shigehiro, Ishioka, Japan
Shigematsu, Nobuharu, Tsukuba, Japan
Yoshimura, Seiji, Tsukuba, Japan
Okada, Satoshi, Kyoto, Japan
Hemmi, deceased, Keiji, late of Tsukuba, Japan by Mitsue Hemmi, heir
Tanaka, Hirokazu, Takarazuka, Japan
Otsuka, Takanao, Tsukuba, Japan
Tsurumi, Yasuhisa, Tsukuba, Japan
Okamoto, Masanori, Osaka, Japan
Okuhara, Masakuni, Tsukuba, Japan
Fukami, Naoki, Ibaraki, Japan
PA Fujisawa Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6110933 20000829
WO 9519959 19950727 <--
AI US 1996-669395 19961112 (8)
WO 1995-JP68 19950123
19961112 PCT 371 date
19961112 PCT 102(e) date
PRAI GB 1994-1268 19940124
GB 1994-21962 19941031
DT Utility
FS Granted
EXNAM Primary Examiner: Dodson, Shelley A.; Assistant Examiner: Qazi, Sabiha N.
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2896
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a novel fatty acid derivative of the

following formula: ##STR1## wherein R.sup.1 is acyl group, etc.;

R.sup.2 is acyl(lower)alkyl;

R.sup.3 is lower alkyl, etc.;

R.sup.4 is hydrogen, etc.; and

X is --O--, etc;

and a pharmaceutically acceptable salt thereof, which is useful as a medicament; the processes for the preparation of said fatty acid derivative or a salt thereof; a pharmaceutical composition comprising said fatty acid derivative or a pharmaceutically acceptable salt thereof; etc.

L4 ANSWER 9 OF 64 USPATFULL on STN
AN 2000:41034 USPATFULL
TI Thienopyridine derivatives and their use
IN Sohda, Takashi, Takatsuki, Japan
Makino, Haruhiko, Hyogo, Japan
Baba, Atsuo, Ashiya, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6046189 20000404
WO 9740050 19971030 <--
AI US 1997-860452 19970626 (8)
WO 1997-JP1413 19970423
19970626 PCT 371 date
19970626 PCT 102(e) date
PRAI JP 1996-105916 19960425
JP 1996-105917 19960425
DT Utility
FS Granted
EXNAM Primary Examiner: Rotman, Alan L.
LREP Foley & Lardner
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3340
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There is disclosed a compound of the formula (A): ##STR1## wherein W is C-G or C-G' (G is optionally esterified carboxyl; and G' is halogen); X is oxygen, optionally oxidized sulfur or --(CH.sub.2).sub.q -- (q is 0 to 5); R is optionally substituted amino or heterocyclic group; the ring B is optionally substituted nitrogen-containing 5- to 7-membered ring; L is hydrogen, optionally substituted hydrocarbon residue, optionally substituted acyl, optionally substituted carbamoyl, optionally substituted thiocarbamoyl or optionally substituted sulfonyl provided that, when W is C-G, L is hydrogen, optionally substituted acyl, optionally substituted carbamoyl, optionally substituted alkoxycarbonyl, optionally substituted thiocarbamoyl or optionally substituted sulfonyl; n is 0 or 1; the ring A may have a substituent. A process for producing the compound (A) and a pharmaceutical composition containing the compound (A) are also disclosed. The pharmaceutical composition is useful for an anti-inflammatory drug, particularly, a drug for preventing or treating arthritis, a drug for inhibiting bone resorption, immunosuppressant or the like.

L4 ANSWER 10 OF 64 USPATFULL on STN
AN 2000:15674 USPATFULL
TI Metalloproteinase inhibitors
IN Miller, Andrew, Oxford, United Kingdom

Whittaker, Mark, Oxford, United Kingdom
Beckett, Raymond Paul, Oxford, United Kingdom
PA Britsh Biotech Pharmaceuticals Limited, Oxford, United Kingdom (non-U.S. corporation)
PI US 6022898 20000208
WO 9535276 19951228 <--
AI US 1996-765146 19961223 (8)
WO 1995-GB1465 19950622
19961223 PCT 371 date
19961223 PCT 102(e) date
PRAI GB 1994-12514 19940622
GB 1995-6107 19950324
DT Utility
FS Granted
EXNAM Primary Examiner: Kumar, Shailendra
LREP Banner & Witcoff, Ltd.
CLMN Number of Claims: 53
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1301
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of general formula (II), wherein X is a hydroxamic or carboxylic acid group, Y is sulphonyl and R.sub.1 and R.sub.2 as defined in the claims are matrix metalloproteinase inhibitors. ##STR1##

L4 ANSWER 11 OF 64 USPATFULL on STN
AN 1999:170588 USPATFULL
TI Perfluoroalkyl ketone inhibitors of elastase and processes for making the same
IN Curran, Timothy T., Chester, NY, United States
Burkhart, Joseph P., Plainfield, IN, United States
Angelastro, Michael R., Mason, OH, United States
Peet, Norton P., Cincinnati, OH, United States
Metz, Jr., William A., Loveland, OH, United States
PA Hoechst Marion Roussel, Inc., Bridgewater, NJ, United States (U.S. corporation)
PI US 6008196 19991228
WO 9533762 19951214 <--
AI US 1996-737905 19961122 (8)
WO 1995-US5363 19950501
19961122 PCT 371 date
19961122 PCT 102(e) date
RLI Continuation of Ser. No. US 1994-327520, filed on 20 Oct 1994, now patented, Pat. No. US 5403052 which is a continuation-in-part of Ser. No. US 1994-252857, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Celsa, Bennett
LREP Gupta, Balaram
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1792
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compounds which are inhibitors of elastase, particularly human neutrophil elastase, and to novel processes for making the same. As inhibitors of human neutrophil elastase, the compounds are useful in the treatment of a patient afflicted with a neutrophil associated inflammatory disease.

L4 ANSWER 12 OF 64 USPATFULL on STN
AN 1999:167048 USPATFULL

TI IL-8 receptor antagonists
IN Widdowson, Katherine Louisa, King of Prussia, PA, United States
Veber, Daniel Frank, Ambler, PA, United States
Jurewicz, Anthony Joseph, Royersford, PA, United States
Hertzberg, Robert Philip, Downingtown, PA, United States
Rutledge, Jr., Melvin Clarence, Lansdale, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 6005008 19991221
WO 9625157 19960822 <--
AI US 1997-894291 19970815 (8)
WO 1996-US2260 19960216
19970815 PCT 371 date
19970815 PCT 102(e) date
DT Utility
FS Granted
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Simon, Soma G., Dinner, Dara L., Kinzig, Charles M.
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4760
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to the novel use of phenyl ureas in the treatment of disease states mediated by the chemokine, Interleukin-8 (IL-8).

L4 ANSWER 13 OF 64 USPATFULL on STN
AN 1999:155727 USPATFULL
TI Pyrrolopyrrolone derivatives as inhibitors of neutrophil elastase
IN Dowle, Michael Dennis, Ware, United Kingdom
Finch, Harry, Letchworth, United Kingdom
Harrison, Lee Andrew, Biggleswade, United Kingdom
Inglis, Graham George, Kingswood, United Kingdom
Johnson, Martin Redpath, Royston, United Kingdom
Macdonald, Simon John Fawcett, Benington, United Kingdom
Shah, Pritom, Biggleswade, United Kingdom
Smith, Robin Andrew, St. Albans, United Kingdom
PA Glaxo Wellcome Inc., Research Triangle Park, NC, United States (U.S. corporation)
PI US 5994344 19991130
WO 9736903 19971009 <--
AI US 1998-155323 19980925 (9)
WO 1997-EP1530 19970326
19980925 PCT 371 date
19980925 PCT 102(e) date
PRAI GB 1996-6508 19960328
GB 1996-23001 19961105
DT Utility
FS Granted
EXNAM Primary Examiner: Stockton, Laura L.
LREP Riek, James P.
CLMN Number of Claims: 32
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6230
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There are described according to the invention compounds of formula (I) (relative stereochemistry indicated), wherein R.sub.1, R.sub.2, R.sub.3 and X are as defined in the specification, together with processes for preparing them, compositions containing them and their use as pharmaceuticals. Compounds of formula (I) are indicated inter alia for the treatment of chronic bronchitis.

L4 ANSWER 14 OF 64 USPATFULL on STN
AN 1999:151245 USPATFULL
TI Benzopyran derivatives having leukotriene-antagonistic action
IN Carganico, Germano, Piode, Italy
Casellas, David Mauleon, Rubi, Spain
Avellana, Jaime Pascual, L'Hospitalet del Llobregat, Spain
Garcia Perez, M. Luisa, El Masnou, Spain
Benet, Albert Palomer, Girona, Spain
PA Laboratorios Menarini S.A., Badalona, Spain (non-U.S. corporation)
PI US 5990142 19991123
WO 9734885 19970925 <--
AI US 1998-142922 19981015 (9)
WO 1997-EP1418 19970320
19981015 PCT 371 date
19981015 PCT 102(e) date
PRAI ES 1996-682 19960321
DT Utility
FS Granted
EXNAM Primary Examiner: Stockton, Laura L.
LREP Griffin, Butler, Whisenhunt & Szipl, LLP
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2950
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel 4-oxo-4H-1-benzopyran compounds containing benzyloxymethyl, 3-phenylpropyl, or other araliphatic substituents in their 8-position. These compounds show a leukotriene-antagonistic activity. The compounds are characterized by good oral adsorption. The compounds of the present invention may be used as anti-inflammatory and antiallergic medicaments, and in the treatment of cardiovascular diseases.

L4 ANSWER 15 OF 64 USPATFULL on STN
AN 1999:7495 USPATFULL
TI Arylsulfonyl hydroxamic acid derivatives as MMP and TNF inhibitors
IN Piscopio, Anthony, Longmount, CO, United States
Rizzi, James P., Niwot, CO, United States
PA Pfizer Inc, New York, NY, United States (U.S. corporation)
PI US 5861510 19990119
WO 9633172 19961024 <--
AI US 1997-930665 19971007 (8)
WO 1995-IB279 19950420
19971007 PCT 371 date
19971007 PCT 102(e) date
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Richardson, Peter C., Ginsburg, Paul H., Holtrust, Gezina
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the formula ##STR1## wherein R.sup.1, R.sup.2 R.sup.3, R.sup.4 R.sup.5, R.sup.6, R.sup.7, R.sup.8, R.sup.9 and Ar are as defined above, useful in the treatment of a condition seiected from the group consisting of arthritis, cancer, tisuue ulceration, restenosis, periodontal disease, epidermolysis bullosa, scleritis and other disease characterized by matrix metalloproteinase activity, as well as AIDS, sepsis, septic shock and other diseases involving the production of TNF.

L4 ANSWER 16 OF 64 USPATFULL on STN
AN 1998:82770 USPATFULL
TI IL-8 receptor antagonists
IN Widdowson, Katherine Louisa, King of Prussia, PA, United States
Veber, Daniel Frank, Ambler, PA, United States
Jurewicz, Anthony Joseph, Royersford, PA, United States
Hertzberg, Robert Philip, Downingtown, PA, United States
Rutledge, Jr., Melvin Clarence, Lansdale, PA, United States
PA SmithKline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 5780483 19980714 <--
AI US 1996-701299 19960821 (8)
RLI Continuation-in-part of Ser. No. US 1996-641990, filed on 20 Mar 1996 which is a continuation-in-part of Ser. No. US 1995-390260, filed on 17 Feb 1995, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Jarvis, William R. A.
LREP Dinner, Dara L., Venetianer, Stephen, Lentz, Edward T.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5468
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel compounds and a novel use of phenyl ureas in the treatment of disease scates mediated by the chemokine, Interleukin-8 (IL-8). In particular, this invention relates to the novel compounds of Formula (Ia) and their use in treating chemokine mediated diseases wherein the chemokine binds to an IL-8 a or b receptor. Compounds of Formula (Ia) are represented by the structure: ##STR1## wherein interalia, X is oxygen or sulfur;

Rb is NR.sub.6 R.sub.7, alkcyl, aryl, arylC.sub.1-4 alkyl, aryl C.sub.2-4 alkenyl, heteroaryl, heteroarylC.sub.1-4 alkyl, heteroarylC.sub.2-4 alkenyl, heterocyclic or heterocyclic C.sub.1-4 alkyl, or a heterocyclic C.sub.2-4 alkenyl moiety, camphor, all of which may be optionally substituted;

R.sub.1 is independently selected from hydrogen; halogen; nitro; cyano; C.sub.1-10 alkyl; halosubstituted C.sub.1-10 alkyl; C.sub.2-10 alkoxy; halosubstituted C.sub.1-10 alkoxy; azide; (CR.sub.8 R.sub.8)q S(O).sub.t R.sub.4 ; hydroxy; hydroxy substituted C.sub.1-4 alkyl; aryl; aryl C.sub.1-4 alkyl; aryl C.sub.2-10 alkenyl; aryloxy; aryl C.sub.1-4 alkyloxy; heteroaryl; heteroarylalkyl; heteroaryl C.sub.2-10 alkenyl; heteroaryl C.sub.1-4 alkyloxy; heterocyclic; heterocyclic C.sub.1-4 alkyl; heterocyclicC.sub.1-4 alkyloxy; heterocyclic C.sub.2-10 alkenyl;

q is 0 or an integer having a value of 1 to 10; n is an integer having a value of 1 to 3;

m is an integer having a value of 1 to 3;

Y is hydrogen; halogen; nitro; cyano; halosubstituted C.sub.1-10 alkyl; C.sub.1-10 alkyl; C.sub.2-10 alkenyl C.sub.1-10 alkoxy; halosubstituted C.sub.1-10 alkoxy; azide; (CR.sub.8 R.sub.8)qS(O).sub.t R.sub.4, (CR.sub.8 R.sub.8)qOR.sub.4 ; hydorxy; hydroxy substituted C.sub.1-4 alkyl; aryl; aryl C.sub.1-4 alkyl; aryloxy; arylC.sub.1-4 alkyloxy; aryl C.sub.2-10 alkenyl; heteroaryl; heteroarylalkyl; heteroaryl C.sub.1-4 alkyloxy; heteroaryl C.sub.2-10 alkenyl; heterocyclic, heterocyclic C.sub.1-4 alkyl; heterocyclicC.sub.2-10 alkenyl;

or a pharmaceutically acceptable salt thereof.

L4 ANSWER 17 OF 64 USPATFULL on STN
AN 1998:61643 USPATFULL
TI Integrin receptor antagonists
IN Jadhav, Prabhakar Kondaji, Wilmington, DE, United States
Petraitis, Joseph James, Glenmoore, PA, United States
Batt, Douglas Guy, Wilmington, DE, United States
PA The DuPont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)
PI US 5760028 19980602 <--
AI US 1996-770538 19961220 (8)
PRAI US 1995-9088P 19951222 (60)
US 1996-25699P 19960809 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Grumbling, Matthew V.
LREP Ferguson, Blair Q.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 9776
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel heterocycles including 3-[1-[3-(imidazolin-2-ylamino)propyl]indazol-5-ylcarbonylamino]-2-(benzyloxycarbonylamino)propionic acid, which are useful as antagonists of the .alpha..sub.v .beta..sub.3 integrin and related cell surface adhesive protein receptors, to pharmaceutical compositions containing such compounds, processes for preparing such compounds, and to methods of using these compounds, alone or in combination with other therapeutic agents, for the inhibition of cell adhesion, the treatment of angiogenic disorders, inflammation, bone degradation, cancer metastasis, diabetic retinopathy, thrombosis, restenosis, macular degeneration, and other conditions mediated by cell adhesion and/or cell migration and/or angiogenesis.

L4 ANSWER 18 OF 64 USPATFULL on STN
AN 1998:54894 USPATFULL
TI Method of modifying angiotensin receptor activity for mediation of pain
IN dePadova, Anthony S., 49 Dexter Dr. North, Basking Ridge, NJ, United States 07920
PI US 5753651 19980519 <--
WO 9529674 19951109 <--
AI US 1996-727553 19961025 (8)
WO 1995-US5312 19950428
19961023 PCT 371 date
19961023 PCT 102(e) date
RLI Continuation-in-part of Ser. No. US 1994-235468, filed on 29 Apr 1994, now patented, Pat. No. US 5464854
DT Utility
FS Granted
EXNAM Primary Examiner: Jordan, Kimberly
LREP Hoffmann & Baron, LLP
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 818
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a method of modifying Angiotensin II subtype 1 (AT.sub.1) receptor activity for the treatment of premenstrual syndrome (PMS) and the symptoms associated therewith, and further relates to a method for the treatment of acute or chronic pain mediated

by the sympathetic nervous system. The treatment includes the administration of an effective amount of an AT.sub.1 antagonist. AT.sub.1 antagonists are drugs that are capable of blocking AT.sub.1 receptors present within the body throughout the central nervous system including the hypothalamus. By blocking the AT.sub.1 receptor activity, hypothalamic nerve activity, and therefore, sympathetic nerve activity are modulated. Thus, an effective method for treating sympathetically mediated pain is provided, as well as an effective method for treating PMS. The AT.sub.1 antagonist can be used alone or in combination with other drug therapies, for instance, non-steroidal anti-inflammatory drugs, antidepressants, opiod drugs, angiotensin converting enzyme inhibitors, and diuretics.

L4 ANSWER 19 OF 64 USPATFULL on STN
AN 1998:51608 USPATFULL
TI Pharmaceutically active compounds
IN Girijavallabhan, Viyyoor M., Parsippany, NJ, United States
Ganguly, Ashit K., Upper Montclair, NJ, United States
Pinto, Patrick A., Mine Hill, NJ, United States
Versace, Richard W., Wanaque, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 5750532 19980512 <--
AI US 1995-453723 19950530 (8)
RLI Division of Ser. No. US 1993-169809, filed on 17 Dec 1993, now patented, Pat. No. US 5459144 which is a continuation-in-part of Ser. No. US 1989-376476, filed on 7 Jul 1989, now abandoned which is a continuation-in-part of Ser. No. US 1986-940125, filed on 10 Dec 1986, now patented, Pat. No. US 4851423
DT Utility
FS Granted
EXNAM Primary Examiner: Berch, Mark L.
LREP Boxer, Matthew, Maitner, John J.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2478
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The disclosed invention is compounds represented by the formula ##STR1## and pharmacetically acceptable acid salts thereof, wherein each Z is independently tetiary butyl, phenyl, naphthyl or adamantyl; substituted phenyl, wherein the substituents are one or more of halogen, lower alkoxy, phenoxy, nitrile, nitro, phenylsulfonyl, loweralkyl-sulfonyl, oxazol-2-yl, lower alkanoyl, benzoyl, lower alkoxycarbonyl, lower alkyl, lower alkylthio, phenyl, phenylaminothiocarbonyl, or lower alkylaminothiocarbonyl, hydroxyiminoloweralkyl hydroxyloweralkyl or **carbonyl**; or 4 or 6 membered unsubstituted or substituted heterocyclic ring containing at least one nitrogen with the remaining member of the ring being at least one carbon, and optionally sulfur or oxygen,

X and Y are each independently a bond, ##STR2## each Q is independently a divalent substituted or unsubstituted, straight or branched chain lower alkanediyl, lower alkanediyl-cycloalkanediyl-lower alkanediyl, lower alkenediyl, lower alkynediyl, phenylene, dihydrofurandiyl, loweralkanediyl-dihydrofurandiyl-loweralkanediyl, tetrahydrofurandiyl, tetrahydropyrandiyl, loweralkanediyl-tetrahydropyrandiyl-loweralkanediyl or, loweralkanediyl-tetrahydrofurandiyl-loweralkanediyl;

W is a monovalent substituted or unsubstituted aryl group or a heterocyclic single or fused ring containing from 4 to 10 ring atoms, at least one hetero atom of which is a nitrogen atom and the remaining ring atoms being at least one carbon and optionally sulfur or oxygen, with

the proviso that W cannot be substituted or unsubstituted isoxazolyl, and with the further proviso that when Z is 2-chloro-4-methoxyphenyl, X is --O--, Q is C.sub.5 -C.sub.7 alkanediyl and Y is a bond, W is not imidazolyl substituted at positions 2, 4 and 5 with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyloweralkyl, nitro, loweralkoxycarbonyl, lower alkyl and amino methylene;

W' is divale W.

The compound is have antiviral activity, antiinflammatory activity and are PAF inhibitors.

L4 ANSWER 20 OF 64 USPATFULL on STN
AN 1998:25212 USPATFULL
TI Peptide derivatives
IN Edwards, Philip Duke, Claymont, DE, United States
Schwartz, John Anthony, Wilmington, DE, United States
Stein, Mark Morris, Wilmington, DE, United States
Trainor, Diane Amy, Glen Mills, PA, United States
Wildonger, Richard Alan, Newark, DE, United States
PA Zeneca Inc., Wilmington, DE, United States (U.S. corporation)
PI US 5726158 19980310 <--
AI US 1995-467333 19950606 (8)
RLI Continuation of Ser. No. US 1990-482617, filed on 21 Feb 1990, now abandoned which is a division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Johnson, Jerry D.
LREP Hohenschutz, Liza D.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5961
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

L4 ANSWER 21 OF 64 USPATFULL on STN
AN 1998:19722 USPATFULL
TI Substituted benzylamino nitrogen containing non-aromatic heterocycles
IN Howard, Harry R., Bristol, CT, United States
Nakane, Masami, Nagoya, Japan
Ikunaka, Masaya, Chita, Japan
Satake, Kunio, Handa, Japan
Rosen, Terry J., East Lyme, CT, United States
Lowe, III, John A., Stonington, CT, United States
O'Neill, Brian T., Westbrook, CT, United States
Ito, Fumitaka, Chita-gun, Japan
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 5721255 19980224 <--
WO 9404496 19940303 <--
AI US 1995-387765 19950215 (8)

WO 1993-US4063 19930505
19950215 PCT 371 date
19950215 PCT 102(e) date

DT Utility
FS Granted
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Huang, Evelyn
LREP Richardson, Peter C., Ginsburg, Paul H., Creagan, B. Timothy
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2430
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel substituted benzylamino nitrogen containing non-aromatic heterocycles and, specifically, to compounds of the formula ##STR1## wherein W, R.sup.1, R.sup.2, R.sup.3 and A are as defined in the specification, and to intermediates used in the synthesis of such compounds. The novel compounds of formula I are useful in the treatment of inflammatory and central nervous system disorders, as well as other disorders.

L4 ANSWER 22 OF 64 USPATFULL on STN
AN 1998:14942 USPATFULL
TI Substituted imidazoles having anti-cancer and cytokine inhibitory activity
IN Selnick, Harold G., Ambler, PA, United States
Claremon, David A., Maple Glen, PA, United States
Liverton, Nigel J., Harleysville, PA, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5717100 19980210 <--
AI US 1996-717955 19960923 (8)
PRAI US 1995-5063P 19951006 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Aulakh, Charanjit S.
LREP Billups, Richard C., Daniel, Mark R.
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3169
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds represented by formula I: ##STR1## are disclosed. AR represents an aromatic group containing 6-10 atoms; and ##STR2## represents a 4 to 6 membered non-aromatic heterocycle containing only one N atom.

A pharmaceutical composition is also included.

Methods of treating cancer and cytokine mediated diseases are also included.

L4 ANSWER 23 OF 64 USPATFULL on STN
AN 1998:7077 USPATFULL
TI Integrin receptor antagonists
IN Voss, Matthew Ernst, Lincoln University, PA, United States
Jadhav, Prabhakar Kondaji, Wilmington, DE, United States
Smallheer, Joanne Marie, Landenberg, PA, United States
Batt, Douglas Guy, Wilmington, DE, United States
Pitts, William John, Conshohocken, PA, United States
Wityak, John, West Grove, PA, United States
PA The DuPont Merck Pharmaceutical Company, Wilmington, DE, United States (U.S. corporation)

PI US 5710159 19980120 <--
AI US 1996-647132 19960509 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: McKane, Joseph
LREP Ferguson, Blair Q.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6665
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to novel heterocycle compounds including but not limited to 3-[3-[3-(imidazolin-2-yl amino)propyloxy]isoxazol-5-ylcarbonylamino]-2-(benzyloxycarbonylamino)-propionic acid, which are useful as antagonists of the .alpha..sub.v .beta..sub.3 and related integrin receptors, to pharmaceutical compositions containing such compounds, processes for preparing such compounds, and to methods of using these compounds, alone or in combination with other therapeutic agents, for the inhibition of cell adhesion and the treatment of angiogenic disorders, inflammation, bone degradation, tumors, metastases, thrombosis, and other cell aggregation-related conditions.

L4 ANSWER 24 OF 64 USPATFULL on STN
AN 1998:7071 USPATFULL
TI Tetrazole compound
IN Ohmoto, Kazuyuki, Osaka, Japan
Tanaka, Makoto, Osaka, Japan
Miyazaki, Tohru, Osaka, Japan
Ohno, Hiroyuki, Osaka, Japan
PA Ono Phramaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5710153 19980120 <--
AI US 1996-712393 19960911 (8)
PRAI JP 1995-259277 19950912
DT Utility
FS Granted
EXNAM Primary Examiner: McKane, Joseph
LREP Sughrue, Mion, Zinn, Macpeak & Seas, PLLC
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4968
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A tetrazole derivatives of formula (I) ##STR1## a non-toxic salt thereof, an acid addition salt thereof or a hydrate thereof which has an inhibitory effect on interleukin-1.beta. converting enzyme (ICE).

L4 ANSWER 25 OF 64 USPATFULL on STN
AN 97:118015 USPATFULL
TI Acylated enol derivatives as prodrugs of elastase inhibitors
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., West Chester, OH, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Merrell Pharmaceuticals Inc., Cincinnati, OH, United States (U.S. corporation)
PI US 5698523 19971216 <--
AI US 1996-670136 19960625 (8)
RLI Continuation of Ser. No. US 1995-420859, filed on 19 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-252798, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Stockton, Laura L.

LREP Boudreaux, William R.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of known elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema or as prodrugs of compounds which are useful in the treatment of said diseases.

L4 ANSWER 26 OF 64 USPATFULL on STN
AN 97:86601 USPATFULL
TI Aminophenylphosphonic acid compounds
IN Cordi, Alex, Suresnes, France
Desos, Patrice, Courbevoie, France
Morris, Angela D., Montigny Le Bretonneux, France
Atassi, Ghanem, Saint Cloud, France
PA Adir et Compagnie, Courbevoie, France (non-U.S. corporation)
PI US 5670493 19970923 <--
AI US 1996-684469 19960719 (8)
PRAI FR 1995-8821 19950721
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Ambrose, Michael G.
LREP The Firm of Gordon W. Hueschen
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1837
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of formula (I): ##STR1## in which: R.sub.1, R.sub.2, which may be identical or different, represent hydrogen or halogen, or alkyl, alkoxy, nitro or trihalomethyl,

X represents CO, SO.sub.2 or CH.sub.2,

A.sub.1 represents any one of the groups as defined in the description,

A.sub.2 represents --(CH.sub.2).sub.n or --CH.dbd.CH--,

R.sub.3, R.sub.4, which may be identical or different, represent hydrogen or alkyl,

its isomers as well as its addition salts with a pharmaceutically acceptable base and medicinal product containing the same are useful as angiogenesis inhibitors.

L4 ANSWER 27 OF 64 USPATFULL on STN
AN 97:66140 USPATFULL
TI 2-saccharinylmethyl heterocyclic carboxylates useful as proteolytic enzyme inhibitors and compositions and method of use thereof
IN Dunlap, Richard Paul, Penfield, NY, United States
Hlasta, Dennis John, Clifton Park, NY, United States
Desai, Ranjit Chimanlal, Colonie, NY, United States
Latimer, Lee Hamilton, Brighton, NY, United States
Subramanyam, Chakrapani, East Greenbush, NY, United States
Court, John Joseph, Colonie, NY, United States
Bell, Malcolm Rice, East Greenbush, NY, United States
Kumar, Virendra, Colonie, NY, United States

PA Sanofi, S.A., Paris, France (non-U.S. corporation)
PI US 5652254 19970729 <--
AI US 1996-705097 19960828 (8)
RLI Division of Ser. No. US 1995-445247, filed on 19 May 1995, now patented, Pat. No. US 5563163 which is a division of Ser. No. US 1994-287681, filed on 9 Aug 1994, now patented, Pat. No. US 5488062, issued on 30 Jan 1996 which is a division of Ser. No. US 1993-109411, filed on 19 Aug 1993, now patented, Pat. No. US 5376653, issued on 27 Dec 1994 which is a continuation of Ser. No. US 1991-816621, filed on 30 Dec 1991, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Cross, Laura R.
LREP Dupont, Paul E.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2781
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 4-R.sup.4 -R.sup.5 -2-Saccharinylmethyl heterocyclic carboxylates, useful in the treatment of degenerative diseases, are prepared by reacting a 4-R.sup.4 -R.sup.5 -2-halomethylsaccharin with either a heterocyclic carboxylic acid in the presence of an acid-acceptor or the alkali metal salt of a heterocyclic carboxylic acid.

L4 ANSWER 28 OF 64 USPATFULL on STN
AN 97:45039 USPATFULL
TI Sulfonamide aminomethylene derivatives as immunosuppressants
IN Connell, Richard D., New Haven, CT, United States
Osterman, David G., Glastonbury, CT, United States
Katz, Michael E., Wallingford, CT, United States
Dally, Robert D., Branford, CT, United States
PA Miles Inc., West Haven, CT, United States (U.S. corporation)
PI US 5633277 19970527 <--
AI US 1995-535507 19950926 (8)
RLI Continuation of Ser. No. US 1993-15502, filed on 9 Feb 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Wu, Shean C.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1014
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds which suppress human T-lymphocyte proliferation are disclosed. The active compounds essentially contain at least the following structure: ##STR1##

L4 ANSWER 29 OF 64 USPATFULL on STN
AN 97:18176 USPATFULL
TI Indole derivatives
IN Macor, John E., New York, NY, United States
Wythes, Martin J., New York, NY, United States
PA Pfizer Inc, New York, NY, United States (U.S. corporation)
PI US 5607951 19970304 <--
AI US 1995-470392 19950606 (8)
RLI Continuation-in-part of Ser. No. US 1995-401647, filed on 10 Mar 1995, now abandoned which is a continuation of Ser. No. US 1993-53930, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-39244, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1990-597928, filed on 15 Oct 1990,

now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Powers, Fiona T.
LREP Richardson, Peter C., Ginsburg, Paul H., Fuller, Jr., Grover F.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3077
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula ##STR1## wherein the substituents are as defined in the description and the pharmaceutically acceptable salts thereof are new. These compounds are useful psychotherapeutics and are potent serotonin (5-HT.sub.1) agonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania and headache associated with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. The compounds can also be used as centrally acting antihypertensives and vasodilators. A process for forming indoles by transition metal catalyzed cyclization of a dihalogenated intermediate.

L4 ANSWER 30 OF 64 USPATFULL on STN
AN 97:7945 USPATFULL
TI 2-saccharinylmethyl aryl carboxylates useful as proteolytic enzyme inhibitors and compositions and method of use thereof
IN Dunlap, Richard P., Penfield, NY, United States
Boaz, Neil W., Waterloo, NY, United States
Mura, Albert J., Rochester, NY, United States
Kumar, Virendra, Tredyffrin Township, Chester County, PA, United States
Subramanyam, Chakrapani, Towamencin Township, Montgomery County, PA, United States
Desai, Ranjit C., Towamencin Township, Montgomery County, PA, United States
Hlasta, Dennis J., Lower Salford Township, Montgomery County, PA, United States
Saindane, Manohar T., Upper Providence Township, Montgomery County, PA, United States
Bell, Malcolm R., East Greenbush, NY, United States
Court, John J., West Norriton, PA, United States
Farrell, Robert P., East Vincent, PA, United States
PA Sterling Winthrop, Inc., New York, NY, United States (U.S. corporation)
PI US 5597841 19970128 <--
AI US 1995-445118 19950519 (8)
RLI Division of Ser. No. US 1993-116416, filed on 3 Sep 1993, now patented, Pat. No. US 5512589 which is a continuation-in-part of Ser. No. US 1992-965593, filed on 23 Oct 1992, now patented, Pat. No. US 5306818 which is a continuation-in-part of Ser. No. US 1992-860340, filed on 30 Mar 1992, now patented, Pat. No. US 5250696 which is a division of Ser. No. US 1991-782016, filed on 24 Oct 1991, now patented, Pat. No. US 5128339, issued on 7 Jul 1992 which is a continuation-in-part of Ser. No. US 1990-608068, filed on 1 Nov 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Cross, Laura R.
LREP Dupont, Paul E.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5269
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 4-R.sup.4 -R.sup.5 -2-Saccharinylmethyl aryl carboxylates, useful in the

treatment of degenerative diseases, are prepared by reacting a 4-R.sup.4 -R.sup.5 -2-halomethylsaccharin with an arylcarboxylic acid in the presence of an acid-acceptor.

L4 ANSWER 31 OF 64 USPATFULL on STN
AN 96:118595 USPATFULL
TI Imidazopyridine derivatives and their use
IN Takatani, Muneo, Kyoto, Japan
Kozai, Yoshio, Toyonaka, Japan
Tomimatsu, Kiminori, Minoo, Japan
Shibouta, Yumiko, Suita, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5587383 19961224 <--
AI US 1995-387010 19950210 (8)
RLI Division of Ser. No. US 1993-74292, filed on 9 Jun 1993, now patented, Pat. No. US 5395839 which is a division of Ser. No. US 1991-736957, filed on 30 Jul 1991, now patented, Pat. No. US 5244908
PRAI JP 1990-202963 19900730
JP 1990-202964 19900730
JP 1991-121277 19910527
JP 1991-140186 19910612
DT Utility
FS Granted
EXNAM Primary Examiner: Dentz, Bernard
LREP Foley & Lardner
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4793
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A calmodulin inhibitory composition containing a compound of the formula (I): ##STR1## as well as an angiogenesis inhibitory composition containing a compound of the formula (1): ##STR2## are disclosed.

L4 ANSWER 32 OF 64 USPATFULL on STN
AN 96:108981 USPATFULL
TI Indole derivatives
IN Macor, John E., New York, NY, United States
Wythes, Martin J., New York, NY, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 5578612 19961126 <--
AI US 1995-469258 19950606 (8)
RLI Continuation-in-part of Ser. No. US 1995-401647, filed on 10 Mar 1995, now abandoned which is a continuation of Ser. No. US 1993-53930, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-39244, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1990-597928, filed on 15 Oct 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Powers, Fiona T.
LREP Richardson, Peter C., Ginsburg, Paul H., Fuller, Jr., Grover F.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3134
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula ##STR1## wherein R.sub.1, R.sub.2, R.sub.3, X and n are as defined in the claims and the pharmaceutically acceptable salts thereof are new. These compounds are useful psychotherapeutics and are potent serotonin (5-HT.sub.1) agonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse,

cluster headache, migraine, pain, chronic paroxysmal hemicrania and headache associated with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. The compounds can also be used as centrally acting hypertensives and vasodilators. A process for forming indoles by transition metal catalyzed cyclization of dihalogenated intermediate is also disclosed.

L4 ANSWER 33 OF 64 USPATFULL on STN
AN 96:87734 USPATFULL
TI Indole derivatives
IN Macor, John E., New York, NY, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 5559246 19960924 <--
AI US 1995-466650 19950606 (8)
RLI Continuation-in-part of Ser. No. US 1995-401647, filed on 10 Mar 1995, now abandoned which is a continuation of Ser. No. US 1993-53930, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-39244, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1990-597928, filed on 15 Oct 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Powers, Fiona T.
LREP Richardson, Peter C., Ginsburg, Paul H., Fuller, Jr., Grover F.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3084
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula ##STR1## wherein R.sub.1, R.sub.2, R.sub.3, X and n are as defined in the claims and the pharmaceutically acceptable salts thereof are new. These compounds are useful psychotherapeutics and are potent serotonin (5-HT.sub.1) agonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania and headache associated with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. The compounds can also be used as centrally acting hypertensives and vasodilators. A process for forming indoles by transition metal catalyzed cyclization of dihalogenated intermediate is also disclosed.

L4 ANSWER 34 OF 64 USPATFULL on STN
AN 96:87618 USPATFULL
TI Indole derivatives
IN Macor, John E., New York, NY, United States
Wythes, Martin J., New York, NY, United States
PA Pfizer Inc, New York, NY, United States (U.S. corporation)
PI US 5559129 19960924 <--
AI US 1995-466645 19950606 (8)
RLI Continuation-in-part of Ser. No. US 1995-401647, filed on 10 Mar 1995, now abandoned which is a continuation of Ser. No. US 1993-53930, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-39244, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1990-597928, filed on 15 Oct 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Powers, Fiona T.
LREP Richardson, Peter C., Ginsburg, Paul H., Fuller, Jr., Grover F.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 3044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula ##STR1## wherein R.sub.1, R.sub.2, R.sub.3, X and n are as defined in the claims and the pharmaceutically acceptable salts thereof are new. These compounds are useful psychotherapeutics and are potent serotonin (5-HT.sub.1) agonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania and headache associated with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. The compounds can also be used as centrally acting hypertensives and vasodilators. A process for forming indoles by transition metal catalyzed cyclization of dihalogenated intermediate is also disclosed.

L4 ANSWER 35 OF 64 USPATFULL on STN
AN 96:72892 USPATFULL
TI Indole derivatives
IN Macor, John E., New York, NY, United States
Wythes, Martin J., New York, NY, United States
PA Pfizer Inc., New York, NY, United States (U.S. corporation)
PI US 5545644 19960813 <--
AI US 1995-466644 19950606 (8)
RLI Continuation-in-part of Ser. No. US 1995-401647, filed on 10 Mar 1995, now abandoned which is a continuation of Ser. No. US 1993-53930, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1993-39244, filed on 27 Apr 1993, now abandoned which is a continuation-in-part of Ser. No. US 1990-597928, filed on 15 Oct 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Powers, Fiona T.
LREP Richardson, Peter C., Ginsburg, Paul H., Fuller, Jr., Grover F.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3104
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the formula ##STR1## wherein n is 0, 1, or 2; X is hydrogen, chlorine, bromine or iodine; R.sub.1 is hydrogen; R.sub.3 is selected from hydrogen and C.sub.1 to C.sub.6 linear or branched alkyl; and R.sub.2 is as defined in the specification and the pharmaceutically acceptable salts thereof are useful psychotherapeutics and are potent serotonin (5-HT.sub.1) agonists and may be used in the treatment of depression, anxiety, eating disorders, obesity, drug abuse, cluster headache, migraine, pain, chronic paroxysmal hemicrania and headache associated with vascular disorders, and other disorders arising from deficient serotonergic neurotransmission. The compounds can also be used as centrally acting antihypertensives and vasodilators. A process for forming indoles by transition metal catalyzed cyclization of a dihalogenated intermediate is also disclosed.

L4 ANSWER 36 OF 64 USPATFULL on STN
AN 96:60718 USPATFULL
TI Carboxylate derivatives exhibiting phospholipase A2 inhibitory activity
IN Ohtani, Mitsuaki, Nara, Japan
Kato, Toshiyuki, Suita, Japan
Hori, Yozo, Hirakata, Japan
PA Shionogi & Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5534533 19960709 <--
AI US 1994-313890 19940928 (8)
PRAI JP 1993-246732 19931001
JP 1994-154937 19940706

DT Utility
FS Granted
EXNAM Primary Examiner: Haley, Jacqueline
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2111
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel carboxylate derivatives exhibiting phospholipase A.sub.2 inhibitory activity are disclosed, Specifically, the following compounds of the formula and pharmaceutically acceptable salts thereof are disclosed: ##STR1## wherein A is hydroxy, amino, or lower alkylamino; R.sup.1 to R.sup.12 are independently hydrogen, methyl, methoxy, or hydroxy, provided that all of R.sup.1 to R.sup.12 are not hydrogen; G.sup.1 is a single bond, or a group of --(CH.sub.2).sub.x O(CH.sub.2).sub.y -- wherein x and y are independently 0-5; G.sup.2 is a single bond, oxygen, sulfur, **carbonyl**, etc.; G.sup.3 is alkyl, aryl, or a group of the formula: ##STR2## wherein R.sup.13 and R.sup.14 are independently hydrogen, alkyl, aryl, etc.; or R.sup.13 and R.sup.14 may be taken together with the adjacent nitrogen atom to form a heterocyclic group or a group of the formula: ##STR3## wherein Z is a carbon atom or a nitrogen atom, J, K, and L are independently hydrogen or aryl, etc.; p and q are independently 0, 1, or 2; and n is an integer of 1 to 8.

L4 ANSWER 37 OF 64 USPATFULL on STN
AN 96:36585 USPATFULL
TI 2-saccharinylmethyl aryl carboxylates useful as proteolytic enzyme inhibitors and compositions and method of use thereof
IN Dunlap, Richard P., Penfield, NY, United States
Boaz, Neil W., Waterloo, NY, United States
Mura, Albert J., Rochester, NY, United States
Kumar, Virendra, Tredyffrin Township, Chester County, PA, United States
Subramanyam, Chakrapani, Towamencin Township, Montgomery County, PA, United States
Desai, Ranjit C., Towamencin Township, Montgomery County, PA, United States
Hlasta, Dennis J., Lower Salford Township, Montgomery County, PA, United States
Saindane, Manohar T., Upper Providence Township, Montgomery County, PA, United States
Bell, Malcolm R., East Greenbush, Rensselaer County, NY, United States
Court, John J., West Norriton, Montgomery County, PA, United States
Farrell, Robert P., East Vincent, Chester County, PA, United States
PA Sterling Winthrop Inc., New York, NY, United States (U.S. corporation)
PI US 5512589 19960430 <--
AI US 1993-116416 19930903 (8)
RLI Continuation-in-part of Ser. No. US 1992-965593, filed on 23 Oct 1992, now patented, Pat. No. US 5306818 which is a continuation-in-part of Ser. No. US 1992-860340, filed on 30 Mar 1992, now patented, Pat. No. US 5250696 which is a division of Ser. No. US 1991-782016, filed on 24 Oct 1991, now patented, Pat. No. US 5128339, issued on 7 Jul 1992 which is a continuation-in-part of Ser. No. US 1990-608068, filed on 1 Nov 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann; Assistant Examiner: Cross, Laura R.
LREP Alexander, Michael D., Dupont, Paul E.
CLMN Number of Claims: 33
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 5270
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound having the formula: ##STR1## wherein Ar, R.sup.4 and R.sup.5 are defined herein have pharmaceutical utility as proteolytic enzyme inhibitors.

L4 ANSWER 38 OF 64 USPATFULL on STN
AN 95:41068 USPATFULL
TI 1-alkyl-2-hydroxy-2-trifluoromethyl ethylamines
IN Stein, Mark M., Wilmington, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
PA Zeneca Inc., Wilmington, DE, United States (U.S. corporation)
PI US 5414132 19950509 <--
AI US 1992-940932 19920904 (7)
RLI Division of Ser. No. US 1990-491757, filed on 9 Mar 1990, now patented, Pat. No. US 5194588 which is a division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
LREP Cushman Darby & Cushman
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5536
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

L4 ANSWER 39 OF 64 USPATFULL on STN
AN 95:29652 USPATFULL
TI Derivatives of P-substituted phenyl ester of pivalic acid
IN Imaki, Katsuhiro, Osaka, Japan
Arai, Yoshinobu, Osaka, Japan
Okegawa, Tadao, Osaka, Japan
PA Ono Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5403850 19950404 <--
AI US 1994-235856 19940429 (8)
RLI Division of Ser. No. US 1992-960301, filed on 13 Oct 1992, now patented, Pat. No. US 5336681 which is a continuation of Ser. No. US 1991-681364, filed on 8 Apr 1991, now abandoned which is a division of Ser. No. US 1989-364994, filed on 12 Jun 1989, now patented, Pat. No. US 5017610
PRAI JP 1988-145450 19880613
JP 1989-53541 19890306
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Conrad, III, Joseph M.
LREP Stevens, Davis, Miller & Mosher
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1800

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A derivative of general formula: ##STR1## wherein Y is --SO.sub.2 --or ##STR2## (i) R.sup.1 and R.sup.2, which may the same or different, each represent, (1) --H,

(2) C1-16 alkyl or (3) the formula ##STR3## wherein X is single-bond, --SO.sub.2 --, C1-4 alkylene, C1-4 alkylene substituted by --COOH or ##STR4## is a pyridyl or pyrrolyl ring, n is 1.about.5, R.sup.4 is 1 --H or C1-8 alkyl, 2 C1-14 alkoxy 3 C1-6 alkylthio, 4 --OH, halogen, --NO.sub.2 or trihalomethyl, 5 the formula: --NR.sup.41 R.sup.42 wherein R.sup.41 and R.sup.42 each represents halogen or C1-4 alkyl, 6 tetrazole, 7 --SO.sub.3 H or --CH.sub.2 OH, 8 the formula:--SO.sub.2 NR.sup.41 R.sup.42 9 the formula: --Z.sup.41 --COOR.sup.43 wherein Z.sup.41 is single-bond C1-4 alkylene or C2-4 alkenylene, R.sup.43 is --H C1-4 alkyl or benzyl; or non-toxic salt or an acid addition salt thereof possess inhibitory activity on elastase, and therefore is useful for treating pulmonary emphysema, atherosclerosis and **rheumatoid arthritis** and the like.

L4 ANSWER 40 OF 64 USPATFULL on STN
AN 95:20731 USPATFULL
TI Imidazopyridine derivatives and their use
IN Muneo, Takatani, Kyoto, Japan
Kozai, Yoshio, Toyonaka, Japan
Tomimatsu, Kiminori, Minoo, Japan
Shibouta, Yumiko, Suita, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5395839 19950307 <--
AI US 1993-74292 19930609 (8)
RLI Division of Ser. No. US 1991-736957, filed on 30 Jul 1991, now patented, Pat. No. US 5244908
PRAI JP 1990-202963 19900730
JP 1990-202964 19900730
JP 1991-121277 19910527
JP 1991-140186 19910612
DT Utility
FS Granted
EXNAM Primary Examiner: Dentz, Bernard
LREP Foley & Lardner
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4845
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A calmodulin inhibitory composition containing a compound of the formula (I): ##STR1## as well as an angiogenesis inhibitory composition containing a compound of the formula (1): ##STR2## are disclosed.

L4 ANSWER 41 OF 64 USPATFULL on STN
AN 94:68769 USPATFULL
TI Derivatives of p-substituted phenyl ester of pivalic acid
IN Imaki, Katsuhiro, Osaka, Japan
Arai, Yoshinobu, Osaka, Japan
Okegawa, Tadao, Osaka, Japan
PA Ono Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5336681 19940809 <--
AI US 1992-960301 19921013 (7)
RLI Continuation of Ser. No. US 1991-681364, filed on 8 Apr 1991, now abandoned which is a division of Ser. No. US 1989-364994, filed on 12 Jun 1989, now patented, Pat. No. US 5017610, issued on 21 May 1991
PRAI JP 1988-145450 19880613
JP 1989-53541 19890306

DT Utility
FS Granted
EXNAM Primary Examiner: Rotman, Alan L.
LREP Stevens, Davis, Miller & Mosher
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A derivative of general formula: ##STR1## wherein Y is --SO.sub.2 -- or ##STR2## (i) R.sup.1 and R.sup.2, which may the same or different, each represent, (1) --H, (2) C1-16 alkyl or (3) the formula: --X--A--(R.sup.4)n wherein X is single-bond, --SO.sub.2 --, C1-4 alkylene, C1-4 alkylene substituted by --COOH or ##STR3## --A-- is a pyridyl or pyrrolyl ring, n is 1.about.5, R.sup.4 is 1 --H or C1-8 alkyl, 2 C1-14 alkoxy, 3 C1-6 alkylthio, 4 --OH, halogen, --NO.sub.2 or trihalomethyl, 5 the formula: --NR.sup.41 R.sup.42 wherein R.sup.41 and R.sup.42 each represents halogen or C1-4 alkyl, 6 tetrazole, 7 --SO.sub.3 H or --CH.sub.2 OH, 8 the formula: --SO.sub.2 NR.sup.41 R.sup.42 9 the formula: --Z.sup.41 --COOR.sup.43 wherein Z.sup.41 is single-bond, C1-4 alkylene or C2-4 alkenylene, R.sup.43 is --H, C1-4 alkyl or benzyl;

or non-toxic salt or an acid addition salt thereof possess inhibitory activity on elastase, and therefore is useful for treating pulmonary emphysema, atherosclerosis and **rheumatoid arthritis** and the like.

L4 ANSWER 42 OF 64 USPATFULL on STN
AN 94:57803 USPATFULL
TI Aminobutanoic acid compounds having metalloprotease inhibiting properties
IN McElroy, Andrew B., Durham, NC, United States
Brown, Peter J., Chapel Hill, NC, United States
Drewry, David H., Durham, NC, United States
Salovich, James M., Cary, NC, United States
Schoenen, Frank J., Efland, NC, United States
PA Glaxo, Inc., Research Triangle Park, NC, United States (U.S. corporation)
PI US 5326760 19940705 <--
AI US 1993-31439 19930315 (8)
RLI Continuation-in-part of Ser. No. US 1992-905934, filed on 29 Jun 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Richter, Johann
LREP Smith, Gardiner F. H.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3294
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Aminobutanoic acids of the following formula (I): ##STR1## where R.sup.1-R.sup.5 are a variety of substituents, novel intermediates, a pharmaceutical composition for treating inflammatory diseases, demyelinating diseases, and tumor metastasis, methods for such treatment and processes for preparing compounds of formula (I).

L4 ANSWER 43 OF 64 USPATFULL on STN
AN 94:35693 USPATFULL
TI Tetrahydro 2-saccharinylmerthyl aryl carboxylates
IN Subramanyam, Chakrapani, East Greenbush, NY, United States
Bell, Malcolm R., East Greenbush, NY, United States

PA Sterling Winthrop Inc., New York, NY, United States (U.S. corporation)
PI US 5306818 19940426 <--
AI US 1992-965593 19921023 (7)
RLI Continuation-in-part of Ser. No. US 1992-860340, filed on 30 Mar 1992, now patented, Pat. No. US 5250696 which is a division of Ser. No. US 1991-782016, filed on 24 Oct 1991, now patented, Pat. No. US 5128339, issued on 7 Jul 1992 which is a continuation-in-part of Ser. No. US 1990-608068, filed on 1 Nov 1990, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Alexander, Michael D., Dupont, Paul E.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4677
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 4-R.sup.4 -R.sup.5 -Saccharinylmethyl aryl carboxylates, useful in the treatment of degenerative diseases, are prepared by reacting a 4-R.sup.4 -R.sup.5 -2-halomethylsaccharin with an arylcarboxylic acid in the presence of an acid-acceptor.

L4 ANSWER 44 OF 64 USPATFULL on STN
AN 93:76526 USPATFULL
TI Imidazopyridine derivatives and their pharmaceutical use
IN Takatani, Muneo, Kyoto, Japan
Kozai, Yoshio, Toyonaka, Japan
Tomimatsu, Kiminori, Minoo, Japan
Shibouta, Yumiko, Suita, Japan
PA Takeda Chemical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5244908 19930914 <--
AI US 1991-736957 19910730 (7)
PRAI JP 1990-202963 19900730
JP 1990-202964 19900730
JP 1991-121277 19910527
JP 1991-140186 19910612
DT Utility
FS Granted
EXNAM Primary Examiner: Dentz, Bernard
LREP Wegner, Cantor, Mueller & Player
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A calmodulin inhibitory composition containing a compound of the formula (I): ##STR1## as well as an angiogenesis inhibitory composition containing a compound of the formula (1): ##STR2## are disclosed.

L4 ANSWER 45 OF 64 USPATFULL on STN
AN 93:63173 USPATFULL
TI Tetrahydroisoquinoline amides
IN Skiles, Jerry W., Brookfield, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 5232928 19930803 <--
AI US 1991-792130 19911114 (7)
RLI Continuation of Ser. No. US 1990-536912, filed on 12 Jun 1990, now abandoned which is a continuation of Ser. No. US 1989-385140, filed on 25 Jul 1989, now abandoned
DT Utility
FS Granted

EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Turnipseed, James H.
LREP Frankhouser, D. E., Stempel, A. R., Timbers, M-E. M.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 769
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Tetrahydroisoquinoline amides having the general structure ##STR1## are disclosed, the substituents defined hereinbelow, which amides are useful in inhibiting human leukocyte and neutrophil elastaes.

L4 ANSWER 46 OF 64 USPATFULL on STN
AN 93:50536 USPATFULL
TI N-substituted amides
IN Skiles, Jerry W., Brookfield, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 5221665 19930622 <--
AI US 1991-686918 19910416 (7)
RLI Continuation of Ser. No. US 1989-426069, filed on 27 Oct 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Lester L.
LREP Frankhouser, D. E., Stempel, A. R., Timbers, M-E. M.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB N-substituted amides which inhibit hydrolysis of elastin, are described, which compounds are tri-and di- fluoromethyl ketone amide and non-naturally occurring n-substituted amino acids derivatives.

L4 ANSWER 47 OF 64 USPATFULL on STN
AN 93:20683 USPATFULL
TI Aminoalcohol intermediates for peptide derivatives
IN Edwards, Philip D., Claymont, DE, United States
Schwartz, John A., Wilmington, DE, United States
Stein, Mark M., Wilmington, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
Wildonger, Richard A., Newark, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 5194588 19930316 <--
AI US 1990-491757 19900309 (7)
RLI Division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Lester L.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5515
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone

substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

L4 ANSWER 48 OF 64 USPATFULL on STN
AN 93:1373 USPATFULL
TI Treatment of autoimmune inflammatory, and psoriatic diseases with heterocyclic aminoalkyl esters of mycophenolic acid and derivatives
IN Nelson, Peter H., Los Altos, CA, United States
Gu, Chee-Liang L., Sunnyvale, CA, United States
Allison, Anthony C., Belmont, CA, United States
Eugui, Elsie M., Belmont, CA, United States
Lee, William A., Menlo Park, CA, United States
PA Syntex (U.S.A.) Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5177072 19930105 <--
AI US 1991-809084 19911209 (7)
RLI Continuation of Ser. No. US 1989-358775, filed on 30 May 1989, now abandoned which is a division of Ser. No. US 1988-160212, filed on 25 Feb 1988, now patented, Pat. No. US 4861776 which is a division of Ser. No. US 1987-99950, filed on 23 Sep 1987, now patented, Pat. No. US 4748173 which is a division of Ser. No. US 1987-8909, filed on 30 Jan 1987, now patented, Pat. No. US 4727069
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Mary C.; Assistant Examiner: Ambrose, Michael G.
LREP Lowin, David A., Moran, Tom M.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1473
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Heterocyclic aminoalkyl esters of mycophenolic acid, and the derivatives and pharmaceutically acceptable salts thereof, are useful as immunosuppressive agents, anti-inflammatory agents, anti-tumor agents, anti-viral agents, and anti-psoriatic agents.

L4 ANSWER 49 OF 64 USPATFULL on STN
AN 91:82198 USPATFULL
TI Peptide derivatives
IN Edwards, Philip D., Claymont, DE, United States
Schwartz, John A., Wilmington, all, DE, United States
Stein, Mark M., Wilmington, all, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
Wildonger, Richard A., Elmwood, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 5055450 19911008 <--
AI US 1990-493025 19900313 (7)
RLI Division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-5124 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Lester L.; Assistant Examiner: Davenport, Avis
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 6077
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

L4 ANSWER 50 OF 64 USPATFULL on STN
AN 91:40595 USPATFULL
TI Derivatives of p-substituted phenyl ester of pivalic acid
IN Imaki, Katsuhiro, Osaka, Japan
Arai, Yoshinobu, Osaka, Japan
Okegawa, Tadao, Osaka, Japan
PA Ono Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5017610 19910521 <--
AI US 1989-364994 19890612 (7)
PRAI JP 1988-145450 19880613
JP 1989-53541 19890306
DT Utility
FS Granted
EXNAM Primary Examiner: Shippen, Michael L.
LREP Stevens, Davis, Miller & Mosher
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1642
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A derivative of general formula: ##STR1## wherein Y is --SO.sub.2 -- or ##STR2## (i) R.sup.1 and R.sup.2, which may be the same or different, each represent, (1) --H, (2) C1-16 alkyl or (3) the formula: --X-- .circle.A --(R.sup.4).sub.n wherein X is a single-bond, --SO.sub.2 --, C1-4 alkylene, C1-4 alkylene substituted by ##STR3## -- .circle.A -- is carbocyclic or heterocyclic ring, n is 1.about.5, R.sup.4 is (1) --H or C1-8 alkyl, (2) C1-14 alkoxy, (3) C1-6 alkylthio, (4) --OH, halogen, --NO.sub.2 or trihalomethyl, (5) the formula: --NR.sup.41 R.sup.42 wherein R.sup.41 and R.sup.42 each represents halogen or C1-4 alkyl, (6) tetrazole, (7) --SO.sub.3 H or --CH.sub.2 OH, (8) the formula: --SO.sub.2 NR.sup.41 R.sup.42 (9) the formula: --Z.sup.41 --COOR.sup.43 wherein Z.sup.41 is single-bond, C1-4 alkylene or C2-4 alkenylene, R.sup.43 is --H, C1-4 alkyl or benzyl, (10) the formula: --CONR.sup.41 R.sup.42 (11) the formula: --COO--Z.sup.42 --COOR.sup.43 wherein Z.sup.42 is C1-4 alkylene, R.sup.43 is --H, C1-4 alkyl or benzyl, (12) the formula: --COO--Z.sup.42 --CONR.sup.41 R.sup.42 (13) the formula: --OCO--R.sup.45 wherein R.sup.45 is C1-8 alkyl or p-guanidinophenyl, (14) the formula: --CO--R.sup.46 wherein R.sup.46 is C1-4 alkyl, (15) the formula: --O--Z.sup.43 --COOR.sup.450 wherein Z.sup.43 is C1-6 alkylene, R.sup.450 represents a hydrogen, C1-8 alkyl or p-guanidinophenyl, (16) the formula: ##STR4## wherein ##STR5## is an amino acid residue, R.sup.47 is bond, C1-4 alkyl, R.sup.48 is --H or C1-4 alkyl, R.sup.49 is --OH, C1-4 alkoxy, --NH.sub.2, amino substituted by one or two C1-4 alkyl, carbamoylmethoxy or carbamoylmethoxy substituted by one or two C1-4 alkyl at N atom of carbamoyl, wherein ##STR6## is C3-6 heterocyclic ring, (ii) R.sup.1, R.sup.2 and N atom bonded to R.sup.1 and R.sup.2 together represents heterocyclic ring containing at least a N atom(s) and substituted by --COOH or unsubstituted heterocyclic ring containing at least a N atom(s), R.sup.3 is (1) --H, (2) --OH, (3) C1-6 alkyl, (4) halogen, (5) C1-4 alkoxy or (6) C2-5 acyloxy, m is 1-4.

or non-toxic salt or an acid addition salt thereof possess inhibitory

activity on elastase, and therefore is useful for treating and/or preventing agent for pulmonary emphysema, atherosclerosis and **rheumatoid arthritis** and the like.

L4 ANSWER 51 OF 64 USPATFULL on STN
AN 91:36415 USPATFULL
TI 3-arylcarbonyl- and 3-cycloalkyl-**carbonyl**-1-aminoalkyl-1H-indoles
IN Bell, Malcolm R., East Greenbush, NY, United States
PA Sterling Drug Inc., New York, NY, United States (U.S. corporation)
PI US 5013732 19910507 <--
AI US 1990-559787 19900730 (7)
RLI Division of Ser. No. US 1989-409913, filed on 20 Sep 1989 which is a division of Ser. No. US 1988-255305, filed on 11 Oct 1988, now patented, Pat. No. US 4885295 which is a continuation of Ser. No. US 1986-928335, filed on 7 Nov 1986, now abandoned which is a division of Ser. No. US 1985-810942, filed on 19 Dec 1985, now patented, Pat. No. US 4634776 which is a continuation of Ser. No. US 1985-755239, filed on 15 Jul 1985, now patented, Pat. No. US 4581354, issued on 8 Apr 1986 which is a continuation-in-part of Ser. No. US 1984-637931, filed on 6 Aug 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Webb, William G., Dupont, Paul E.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1,6
DRWN No Drawings
LN.CNT 2671
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 3-Arylcarbonyl- and 3-cycloalkylcarbonyl-1-aminoalkyl-1H-indoles, useful as analgesic, anti-rheumatic and anti-inflammatory agents, are prepared by reacting a 3-arylcarbonyl- or 3-cycloalkylcarbonylindole with an aminoalkyl halide in the presence of an acid-acceptor; by reacting a 1-aminoalkyl-1H-indole with an arylcarboxylic acid halide or a cycloalkanecarboxylic acid halide in the presence of a Lewis acid; or by reacting a 3-arylcarbonyl- or 3-cycloalkanecarbonyl-1-tosyloxyalkyl- or haloalkyl-1H-indole with an amine.

L4 ANSWER 52 OF 64 USPATFULL on STN
AN 90:96806 USPATFULL
TI 3-arylcarbonyl- and 3-cycloalkyl-**carbonyl**-1-aminoalkyl-1H-indole pharmaceutical compositions
IN Bell, Malcolm R., East Greenbush, NY, United States
PA Sterling Drug Inc., New York, NY, United States (U.S. corporation)
PI US 4978664 19901218 <--
AI US 1989-409913 19890920 (7)
RLI Division of Ser. No. US 1988-255305, filed on 11 Oct 1988, now patented, Pat. No. US 4885295 which is a continuation of Ser. No. US 1986-928335, filed on 18 Nov 1986, now abandoned which is a division of Ser. No. US 1985-810942, filed on 19 Dec 1985, now patented, Pat. No. US 4634776 which is a continuation of Ser. No. US 1985-755239, filed on 15 Jul 1985, now patented, Pat. No. US 4581354 which is a continuation-in-part of Ser. No. US 1984-637931, filed on 6 Aug 1984, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Webb, William G., DuPont, Paul E.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2674

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB 3-Arylcarbonyl- and 3-cycloalkylcarbonyl-1-aminoalkyl-1H-indoles, useful as analgesic, anti-rheumatic and anti-inflammatory agents, are prepared by reacting a 3-arylcarbonyl- or 3-cycloalkylcarbonylindoe with an aminoalkyl halide in the presence of an acid-acceptor; by reacting a 1-aminoalkyl-1H-indole with an arylcarboxylic acid halide or a cycloalkanecarboxylic acid halide in the presence of a Lewis acid; or by reacting a 3-arylcarbonyl- or 3-cycloalkanecarbonyl-1-tosyloxyalkyl- or haloalkyl-1H-indole with an amine.

L4 ANSWER 53 OF 64 USPATFULL on STN
AN 90:79866 USPATFULL
TI Diphosphonic acid compounds, and pharmaceutical composition comprising the same useful for treating bone diseases
IN Oku, Teruo, Sakuramura, Japan
Todo, Eishiro, Sakuramura, Japan
Kasahara, Chiyoshi, Sakuramura, Japan
Nakamura, Katsuya, Yatabemachi, Japan
Kayakiri, Hiroshi, Sakuramura, Japan
Hashimoto, Masashi, Sakuramura, Japan
PA Fujisawa Pharmaceutical Company, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4963536 19901016 <--
AI US 1989-333953 19890406 (7)
RLI Division of Ser. No. US 1987-42444, filed on 24 Apr 1987, now patented, Pat. No. US 4857513
PRAI GB 1986-10019 19860424
GB 1986-19074 19860805
GB 1987-5347 19870306
DT Utility
FS Granted
EXNAM Primary Examiner: Rotman, Alan L.
LREP Oblon, Spivak, McClelland, Maier & Neustadt
CLMN Number of Claims: 3
ECL Exemplary Claim: 1,3
DRWN No Drawings
LN.CNT 1632
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the formula: ##STR1## wherein R.sup.1 -A- is a group of the formula: ##STR2## in which R.sup.1 is aryl or a heterocyclic group, each of which may be substituted with substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halo(lower)alkyl, acyl, acylamino and halogen, or lower alkyl which may be substituted with a heterocyclic group optionally substituted with acyl, and

X is O or S, and

R.sup.2 is hydrogen or lower alkyl, provided that when R.sup.1 is lower alkyl, then

R.sup.1 -A- is a group of the formula: ##STR3## in which R.sup.1 and X are each as defined above, processes for the preparation thereof and pharmaceutical composition comprising the same.

L4 ANSWER 54 OF 64 USPATFULL on STN
AN 90:36303 USPATFULL
TI Difluoro keto compounds and their use as HLE inhibitors
IN Trainor, Diane A., Glen Mills, PA, United States
Stein, Mark M., Wilmington, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4923890 19900508 <--

AI US 1987-51951 19870519 (7)
RLI Continuation-in-part of Ser. No. US 1987-3993, filed on 16 Jan 1987, now abandoned
PRAI GB 1986-13704 19860605
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Mary C.; Assistant Examiner: Richter, J.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1,10
DRWN No Drawings
LN.CNT 2394
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to selected difluoro compounds of formulae Ia, Ib and Ic (set out hereinafter) which are useful as inhibitors of human leukocyte elastase.

L4 ANSWER 55 OF 64 USPATFULL on STN
AN 90:21543 USPATFULL
TI Peptide derivatives
IN Bergeson, Scott H., Wilmington, DE, United States
Edwards, Philip D., Claymont, DE, United States
Schwartz, John A., Wilmington, DE, United States
Shaw, Andrew, Kennett Square, PA, United States
Stein, Mark M., Wilmington, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
Wildonger, Richard A., Newark, DE, United States
Wolanin, Donald J., Wilmington, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4910190 19900320 <--
AI US 1987-5538 19870120 (7)
RLI Continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Phillips, Delbert R.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5524
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

L4 ANSWER 56 OF 64 USPATFULL on STN
AN 89:92486 USPATFULL
TI Selected difluoro derivatives
IN Trainor, Diane A., Glen Mills, PA, United States
Stein, Mark M., Wilmington, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4880780 19891114 <--
AI US 1987-58079 19870604 (7)
RLI Continuation-in-part of Ser. No. US 1986-872106, filed on 6 Jun 1986, now abandoned

PRAI GB 1985-14436 19850607
GB 1985-14438 19850607
GB 1985-14440 19850607
DT Utility
FS Granted
EXNAM Primary Examiner: Phillips, Delbert R.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention discloses a series of difluoroketone, mono- di- and tri-peptide derivatives of formula Ia, Ib and Ic:

(Formula set out on pages following Examples)
Ia
(Formula set out on pages following Examples)
Ib
(Formula set out on pages following Examples)
Ic

and salts thereof where appropriate, and wherein the radicals are defined hereafter in the specification. The derivatives are useful in inhibiting the action of human leukocyte elastase. There are also disclosed methods and intermediates for the manufacture of, and pharmaceutical compositions comprising, the said derivatives.

L4 ANSWER 57 OF 64 USPATFULL on STN
AN 89:84234 USPATFULL
TI Difluoro peptide compounds
IN Trainor, Diane A., Glen Mills, PA, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4873221 19891010 <--
AI US 1987-51952 19870519 (7)
PRAI GB 1986-13703 19860605
DT Utility
FS Granted
EXNAM Primary Examiner: Phillips, Delbert R.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1691
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to selected difluoro compounds of formulae Ia, Ib and Ic (set out hereinafter) which are useful as inhibitors of human leukocyte elastase.

L4 ANSWER 58 OF 64 USPATFULL on STN
AN 89:72029 USPATFULL
TI Heterocyclic aminoalkyl esters of mycophenolic acid and derivatives thereof, compositions and use
IN Nelson, Peter H., Los Altos, CA, United States
Gu, Chee-Liang L., Sunnyvale, CA, United States
Allison, Anthony C., Belmont, CA, United States
Eugui, Elsie M., Belmont, CA, United States
Lee, William A., Menlo Park, CA, United States
PA Syntex (U.S.A) Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 4861776 19890829 <--

AI US 1988-160212 19880225 (7)
RLI Division of Ser. No. US 1987-99950, filed on 23 Sep 1987, now patented, Pat. No. US 4748173 which is a division of Ser. No. US 1987-8909, filed on 30 Jan 1987, now patented, Pat. No. US 4727069
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Lowin, David A., Moran, Tom M.
CLMN Number of Claims: 11
ECL Exemplary Claim: 1,11
DRWN No Drawings
LN.CNT 1467
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Heterocyclic aminoalkyl esters of mycophenolic acid, and the derivatives and pharmaceutically acceptable salts thereof, are useful as immunosuppressive agents, anti-inflammatory agents, anti-tumor agents, anti-viral agents, and anti-psoriatic agents.

L4 ANSWER 59 OF 64 USPATFULL on STN
AN 89:67459 USPATFULL
TI Diphosphonic acid compounds, processes for the preparation thereof and pharmaceutical composition comprising the same
IN Oku, Teruo, Ibaraki, Japan
Todo, Eishiro, Ibaraki, Japan
Kasahara, Chiyoshi, Ibaraki, Japan
Nakamura, Katsuya, Ibaraki, Japan
Kayakiri, Hiroshi, Ibaraki, Japan
Hashimoto, Masashi, Ibaraki, Japan
PA Fujisiwa Pharmaceutical Co., Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4857513 19890815 <--
AI US 1987-42444 19870424 (7)
PRAI GB 1986-10019 19860424
GB 1986-19074 19860805
GB 1987-5347 19870306
DT Utility
FS Granted
EXNAM Primary Examiner: Evans, J. E.
LREP Oblon, Spivak, McClelland, Maier & Neustadt
CLMN Number of Claims: 8
ECL Exemplary Claim: 1,8
DRWN No Drawings
LN.CNT 1653
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A compound of the formula: ##STR1## wherein R.sup.1 --A-- is a group of the formula: ##STR2## in which R.sup.1 is aryl or a heterocyclic group, each of which may be substituted with substituent(s) selected from the group consisting of lower alkyl, lower alkoxy, lower alkylthio, halo(lower)alkyl, acyl, acylamino and halogen, or lower alkyl which may be substituted with a heterocyclic group optionally substituted with acyl, and

X is O or S, and

R.sup.2 is hydrogen or lower alkyl, provided that when R.sup.1 is lower alkyl, then

R.sup.1 --A-- is a group of the formula: ##STR3## in which R.sup.1 and X are each as defined above, and pharmaceutically acceptable salts thereof, processes for the preparation thereof and pharmaceutical composition comprising the same.

L4 ANSWER 60 OF 64 USPATFULL on STN

AN 89:60890 USPATFULL
TI Pharmaceutically active compounds
IN Girijavallabhan, Viyyoor M., Parsipppany, NJ, United States
Ganguly, Ashit K., Upper Montclair, NJ, United States
Pinto, Patrick A., Mine Hill, NJ, United States
Versace, Richard W., Ringwood, NJ, United States
PA Schering Corporation, Kenilworth, NJ, United States (U.S. corporation)
PI US 4851423 19890725 <--
AI US 1986-940125 19861210 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Ford, John M.
LREP Rosen, Gerald S., Hoffman, Thomas D., Miller, Stephen I.
CLMN Number of Claims: 21
ECL Exemplary Claim: 1,21
DRWN No Drawings
LN.CNT 1758
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The disclosed invention is compounds represented by the formula

Z--X--Q--Y--W, I

Z--X--Q--Y--W'--Y--Q--X--Z II

and pharmaceutically acceptable acid addition salts and quarternary amine salts thereof, wherein

Z is phenyl, naphthyl or adamantyl; substituted phenyl wherein the substituents are one or more of halogen, lower alkoxy, phenoxy, nitrile, nitro, phenylsulfonyl, methylsulfonyl, isoxazol-2-yl, lower alkanoyl, benzoyl, lower alkoxycarbonyl, lower alkyl, loweralkylthio, phenyl, phenylaminothiocarbonyl, or lower alkylaminothiocarbonyl; 5 or 6 membered unsubstituted or substituted heterocyclic ring containing at least one nitrogen and one carbon in the ring, wherein the substituents are one or more of carboxyl, hydroxymethyl, loweralkyl, loweralkylcarbonyl or aryl lower alkyl; or tertiary butyl;

X and Y are each independently a bond, -O-, ##STR1## Q is a divalent substituted or unsubstituted straight or branched chain lower alkanediyl, -lower alkanedinyl- cycloalkanediyl- lower alkanediyl-, lower alkendiyl, lower alkynediyl, phenylene, tetrahydrofurandiyl or tetrahydropyrandiyl;

W is a monovalent substituted or unsubstituted aromatic heterocyclic single or fused ring containing from 5 to 10 ring atoms, at least one hetero atom of which is a nitrogen atom, wherein the substituents are hydroxy, amino, carbamoyl, carboxyl, nitrile, nitro, oxo, lower alkoxy **carbonyl**, halogen, sulfamyl, lower alkyl, lower alkylthio, lower alkoxy, hydroxyloweralkyl, lower alkoxycarbonylloweralkyl, amino loweralkyl, carboxyloweralkyl, guanidino, thioureido, lower alkylsulfonylamino, aminocarbonylloweralkyl, allyloxycarbonylmethyl or carbamoyloxylowralkyl; and

W' is divalent W.

The compounds have antiviral activity, antiinflammatory activity and are PAF inhibitors.

L4 ANSWER 61 OF 64 USPATFULL on STN
AN 88:34372 USPATFULL
TI Heterocyclic aminoalkyl esters of mycophenolic acid and derivatives thereof and pharmaceutical compositions

IN Nelson, Peter H., Los Altos, CA, United States
Gu, Chee-Liang L., Sunnyvale, CA, United States
Allison, Anthony C., Belmont, CA, United States
Eugui, Elsie M., Belmont, CA, United States
Lee, William A., Menlo Park, CA, United States
PA Syntex (U.S.A.) Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 4748173 19880531 <--
AI US 1987-99950 19870923 (7)
RLI Division of Ser. No. US 1987-8909, filed on 30 Jan 1987
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Lowin, David A., Moran, Tom M.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1,7
DRWN No Drawings
LN.CNT 1458
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Heterocyclic aminoalkyl esters of mycophenolic acid, and the derivatives and pharmaceutically acceptable salts thereof, are useful as immunosuppressive agents, anti-inflammatory agents, anti-tumor agents, anti-viral agents, and anti-psoriatic agents.

L4 ANSWER 62 OF 64 USPATFULL on STN
AN 88:11510 USPATFULL
TI Heterocyclic aminoalkyl esters of mycophenolic acid, derivatives thereof and pharmaceutical compositions
IN Nelson, Peter H., Los Altos, CA, United States
Gu, Chee-Liang L., Sunnyvale, CA, United States
Allison, Anthony C., Belmont, CA, United States
Eugui, Elsie M., Belmont, CA, United States
Lee, William A., Menlo Park, CA, United States
PA Syntex (U.S.A.) Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 4727069 19880223 <--
AI US 1987-8909 19870130 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Ramsuer, Robert W.
LREP Lowin, David A., Moran, Tom M.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1,9
DRWN No Drawings
LN.CNT 1450
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Heterocyclic aminoalkyl esters of mycophenolic acid, and the derivatives and pharmaceutically acceptable salts thereof, are useful as immunosuppressive agents, anti-inflammatory agents, anti-tumor agents, anti-viral agents, and anti-psoriatic agents.

L4 ANSWER 63 OF 64 USPATFULL on STN
AN 88:9936 USPATFULL
TI Mycophenolic acid derivatives in the treatment of **rheumatoid arthritis**
IN Nelson, Peter H., Los Altos, CA, United States
Allison, Anthony C., Belmont, CA, United States
Eugui, Elsie M., Belmont, CA, United States
Muchowski, Joseph M., Sunnivale, CA, United States
PA Syntex (U.S.A.) Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 4725622 19880216 <--
AI US 1986-821633 19860123 (6)
DT Utility
FS Granted

EXNAM Primary Examiner: Fan, Jane T.
LREP Wise, Ellen J., Moran, Tom M.
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1204
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of treating **rheumatoid arthritis** which method comprises administering to a mammal in need of such treatment a therapeutically effective amount of a compound of the formula: ##STR1## and the pharmaceutically acceptable salts thereof, wherein:

A is oxygen or sulfur;

R.sup.1 is selected from the group consisting of H, ##STR2## in which Y is oxygen or sulfur:

R.sup.2 is alkyl, haloalkyl or --NR.sup.4 R.sup.5, where R.sup.4 and R.sup.5 are independently H, alkyl, haloalkyl, cycloalkyl, phenyl optionally monosubstituted with halogen, hydroxy, carboxy, chlorocarbonyl, **sulfonylamino**, nitro, cyano, phenyl, alkyl, acyl, alkoxycarbonyl, acylamino, dialkylamino or dialkylaminoethoxycarbonyl, phenyl optionally disubstituted with hydroxy, carboxy, nitro or alkyl, or benzyl optionally substituted with dialkylamino;

n is an integer from 0-6;

R.sup.3 is H alkyl or a pharmaceutically acceptable cation;

Q and R are independently H or --CO.sub.2 R.sup.3 ; and

Z is selected from the group consisting of ##STR3## in which X is oxygen or sulfur,

R.sup.7 is H, alkyl, alkenyl, cycloalkyl, optionally substituted phenyl, optionally substituted benzyl or a pharmaceutically acceptable cation; and

R.sup.8 and R.sup.9 are independently H, alkyl or cycloalkyl, or R.sup.8 and R.sup.9 taken together are --(CH.sub.2).sub.4 --, --(CH.sub.2).sub.5 -- or --(CH.sub.2).sub.2 O(CH.sub.2).sub.2 --;

with the proviso that R.sup.1 and R.sup.7 cannot both be H if X and A are oxygen.

L4 ANSWER 64 OF 64 USPATFULL on STN
AN 81:899 USPATFULL
TI 9,11-Dideoxy-10-oxa-TXB compounds
IN Morton, Jr., Douglas R., Portage, MI, United States
PA The Upjohn Company, Kalamazoo, MI, United States (U.S. corporation)
PI US 4243592 19810106 <--
AI US 1979-19752 19790312 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Love, Ethel G.
LREP Armitage, Robert A.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2666
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present specification discloses novel 9,11-dideoxy- or 9,11,15-trideoxy-10-oxa-thromboxane B compounds, their novel method of preparation and the pharmaceutical compositions and use thereof as antihrombotic, antiinflammatory, and antiasthma agents.

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HIGHEST GRANTED PATENT NUMBER: US6601238
HIGHEST APPLICATION PUBLICATION NUMBER: US2003140390
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ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 29 Jul 2003 (20030729/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2003
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2003

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substance identification.

=> s sulfonylaminocarbonyl and rheumatoid arthritis
           106 SULFONYLAMINOCARBONYL
         19565 RHEUMATOID
         28994 ARTHRITIS
         18220 RHEUMATOID ARTHRITIS
                 (RHEUMATOID(W)ARTHRITIS)
L6          25 SULFONYLAMINOCARBONYL AND RHEUMATOID ARTHRITIS
```

=> d l6 1-25 bib, ab, kwic

L6 ANSWER 1 OF 25 USPATFULL on STN
AN 2003:140917 USPATFULL
TI Novel elastase inhibitors
IN Gallion, Steven L., Woburn, MA, UNITED STATES
Metz, William A., JR., Loveland, OH, UNITED STATES
Burkhart, Joseph P., Plainfield, IN, UNITED STATES
Angelastro, Michael R., Mason, OH, UNITED STATES
Peet, Norton P., Cincinnati, OH, UNITED STATES
PI US 2003096759 A1 20030522
AI US 2000-741536 A1 20001220 (9)
RLI Continuation of Ser. No. US 1996-737235, filed on 20 Nov 1996, ABANDONED A 371 of International Ser. No. WO 1995-US5618, filed on 5 May 1995, UNKNOWN Continuation-in-part of Ser. No. US 1994-252799, filed on 2 Jun 1994, ABANDONED
DT Utility
FS APPLICATION
LREP AVENTIS PHARMACEUTICALS, INC., PATENTS DEPARTMENT, ROUTE 202-206, P.O. BOX 6800, BRIDGEWATER, NJ, 08807-0800
CLMN Number of Claims: 23
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1702
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compounds which are inhibitors of elastase, particularly human neutrophil elastase. The inhibitors are short, synthetic peptides in which the P.sub.2 moiety is substituted with various nitrogen-containing heterocyclic groups. As inhibitors of human neutrophil elastase, the compounds are useful in the treatment of a patient afflicted with a neutrophil associated inflammatory disease.
SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .
SUMM . . . useful as inhibitors of elastase. The compounds of formula I exhibit an anti-inflammatory effect useful in the treatment of gout, **rheumatoid arthritis** and other inflammatory diseases, such as adult respiratory distress syndrome, septicemia, chronic bronchitis, inflammatory bowel disease, disseminated intravascular coagulation, cystic. . .
SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
DETD . . . of formula I will be particularly useful include: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .
DETD . . . elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout and **rheumatoid arthritis**. However, it is understood that the present invention is not limited by any particular theory or proposed mechanism to explain. . .

L6 ANSWER 2 OF 25 USPATFULL on STN

AN 2002:323215 USPATFULL
TI Methods of treating nuclear factor-kappa B mediated diseases and disorders
IN Cornicelli, Joseph Anthony, Ann Arbor, MI, UNITED STATES
Karathanasis, Sotirios K., Saline, MI, UNITED STATES
PI US 2002183384 A1 20021205
AI US 2002-71034 A1 20020208 (10)
PRAI US 2001-268203P 20010212 (60)
DT Utility
FS APPLICATION
LREP Claude F. Purchase, Jr., Warner-Lambert Company, 2800 Plymouth Road, Ann Arbor, MI, 48105
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3473
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of treating a disease or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof. The methods of the present invention are useful for treating, for example, **rheumatoid arthritis**, osteoarthritis, an autoimmune disease, psoriasis, asthma, a cardiovascular disease, an acute coronary syndrome, congestive heart failure, Alzheimer's disease, multiple sclerosis, cancer, type 2 diabetes, metabolic syndrome X, or inflammatory bowel disease.
AB . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof. The methods of the present invention are useful for treating, for example, **rheumatoid arthritis**, osteoarthritis, an autoimmune disease, psoriasis, asthma, a cardiovascular disease, an acute coronary syndrome, congestive heart failure, Alzheimer's disease, multiple sclerosis,. . .
SUMM . . . disease or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to patients in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof.
SUMM . . . effective treatment is available. Noteworthy among the diseases and disorders thought to be responsive to the inhibition of NF-.kappa.B are **rheumatoid arthritis** and osteoarthritis, autoimmune diseases, psoriasis, asthma, cardiovascular diseases such as, for example, atherosclerosis, acute coronary syndromes including myocardial infarction and. . .
SUMM [0010] The present invention provides a method of using a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, to treat diseases and disorders known to be responsive to the inhibition of. . .
SUMM [0011] The following United States patents disclose methods of using certain **sulfonylaminocarbonyl** derivatives as inhibitors of the enzyme acyl-coenzyme A:cholesterol acyltransferase (ACAT) for treating hypercholesterolemia and atherosclerosis:
SUMM [0018] U.S. Pat. No. 6,093,744 discloses methods of using certain **sulfonylaminocarbonyl** derivatives as ACAT inhibitors for regulating plasma cholesterol levels and lowering serum or plasma Lp(a) levels, and for treating hypercholesterolemia,. . .
SUMM [0019] U.S. Pat. No. 6,117,909 discloses methods of using certain **sulfonylaminocarbonyl** derivatives as ACAT inhibitors for lowering serum or plasma Lp(a) levels, and treating cerebrovascular diseases, including stroke, peripheral vascular diseases,. . .
SUMM [0020] U.S. Pat. No. 6,124,309 and its Divisional U.S. Pat. Nos.

6,143,755 and 6,093,719 disclose methods of using a **sulfonylaminocarbonyl** derivative as an ACAT inhibitor in combination with an HMG-CoA reductase inhibitor for restoring endogenous vascular endothelium-dependent activities including improving. . .

SUMM [0022] We have now discovered the ability of certain **sulfonylaminocarbonyl** derivatives to inhibit NF-.kappa.B mediated transcription. Accordingly, the present invention provides a method of treating a disease or a disorder responsive to inhibition of NF-.kappa.B, comprising administering to patients in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof. All that is needed to practice the present invention is to administer to said patients a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, from 1 to 6 times daily for the treatment of **rheumatoid arthritis**, osteoarthritis, autoimmune diseases, psoriasis, asthma, cardiovascular diseases such as, for example, atherosclerosis, acute coronary syndromes including myocardial infarction and unstable. . . 2 diabetes, metabolic syndrome X, and inflammatory bowel disease. Determination of a proper dosage and form of administration of a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, for use in the method of the present invention is well within the. . .

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof.

SUMM [0024] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 5,491,172 and its Divisional U.S. Pat. No. 5,633,287, which are both hereby incorporated herein. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I ##STR1##

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, wherein one of R.sub.1 and R.sub.2 is phenyl; wherein one. . .

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, wherein both R.sub.1 and R.sub.2 are phenyl disubstituted in the. . .

SUMM [0092] In another embodiment of the invention, the method uses a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, wherein R.sub.1 is phenyl disubstituted in the 2,6-positions and R.sub.2. . .

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, selected from:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I named sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl-2,6-bis(1-methylethyl)phenyl ester, or a pharmaceutically acceptable salt thereof.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I named sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl-2,6-bis(1-methylethyl)phenyl ester.

SUMM [0160] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 6,093,744, which is hereby incorporated herein by reference, are also useful in the present. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II ##STR4##

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula I, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II, or a pharmaceutically acceptable salt thereof, wherein:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative of Formula II, or a pharmaceutically acceptable salt thereof, selected from:

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative or a pharmaceutically acceptable salt thereof selected from:

SUMM [0277] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 5,254,715 and its divisional U.S. Pat. No. 5,336,690, which are both hereby incorporated herein. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative selected from:

SUMM [0333] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 5,214,206 and its divisional U.S. Pat. No. 5,288,757, which are both hereby incorporated herein. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative selected from:

SUMM [0374] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 5,198,466 and its divisional U.S. Pat. No. 5,364,882, which are both hereby incorporated herein. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative selected from:

SUMM [0386] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 5,245,068 and its divisional U.S. Pat. No. 5,384,328, which are both hereby incorporated herein. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative selected from:

SUMM [0448] The **sulfonylaminocarbonyl** derivatives disclosed in U.S. Pat. No. 5,254,589 and its continuation U.S. Pat. No. 5,981,595, which are both hereby incorporated herein. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative selected from:

SUMM [0464] The following **sulfonylaminocarbonyl** derivatives are excluded from use in the method of the present invention:

SUMM . . . a method of inhibiting NF-.kappa.B transcription factors in an animal, comprising administering to the animal an NF-.kappa.B inhibiting amount of **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is **rheumatoid arthritis**, osteoarthritis, an autoimmune disease, psoriasis, asthma, a cardiovascular disease, an acute coronary syndrome, congestive heart failure, Alzheimer's disease, multiple sclerosis,. . .

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is **rheumatoid arthritis**, osteoarthritis, systemic lupus erythematosus, Grave's disease, myasthenia gravis, insulin resistance, autoimmune hemolytic anemia, scleroderma with anti-collagen antibodies (Abs), pernicious anemia,. . .

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is **rheumatoid arthritis**.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is osteoarthritis.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is insulin resistance.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is asthma.

SUMM . . . or a disorder responsive to inhibition of nuclear

factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is atherosclerosis.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is myocardial infarction.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is unstable angina.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is congestive heart failure.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is Alzheimer's disease.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is cancer.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is inflammatory bowel disease.

SUMM . . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is multiple sclerosis.

SUMM . . . disease or a disorder, responsive to inhibition of NF-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is type 2 diabetes.

SUMM . . . disease or a disorder, responsive to inhibition of NF-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is metabolic syndrome X.

SUMM . . . disease or a disorder responsive to inhibition of nuclear factor-.kappa.B transciption factors comprising administering to patients in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof.

SUMM [0545] While as mentioned above, some of the **sulfonylaminocarbonyl** derivatives useful in the methods of the present invention are also inhibitors of the enzyme ACAT, and accordingly have demonstrated. . . and plasma cholesterol and Lp(a) regulating activities in vivo, no connection exists betwseen these activities and the ability of the **sulfonylaminocarbonyl** derivatives to inhibit NF-.kappa.B mediated transcription and thereby treat diseases and disorders responsive to inhibition of NF-.kappa.B.

SUMM [0559] The phrase "**sulfonylaminocarbonyl** derivative" means a

compound with one of the following substructure motifs:

Motif Letter	Motif Substructure
A	##STR9##

. . .

SUMM [0561] U.S. Pat. No. 5,254,715 and its divisional U.S. Pat. No. 5,336,690 describe **sulfonylaminocarbonyl** derivatives with substructure motif A.

SUMM [0562] U.S. Pat. No. 5,214,206 and its divisional U.S. Pat. No. 5,288,757 describe **sulfonylaminocarbonyl** derivatives with substructure motif B.

SUMM [0563] U.S. Pat. No. 5,198,466 and its divisional U.S. Pat. No. 5,364,882 describe **sulfonylaminocarbonyl** derivatives with substructure motif C.

SUMM [0564] U.S. Pat. No. 5,245,068 and its divisional U.S. Pat. No. 5,384,328 describe **sulfonylaminocarbonyl** derivatives with substructure motif D.

SUMM [0565] U.S. Pat. No. 5,491,172 and its divisional U.S. Pat. No. 5,633,287, and U.S. Pat. No. 6,093,744 describe **sulfonylaminocarbonyl** derivatives with substructure motif E.

SUMM [0566] U.S. Pat. No. 5,254,589 and its continuation U.S. Pat. No. 5,981,595 describe **sulfonylaminocarbonyl** derivatives with substructure motif F.

SUMM . . . erythematosus, Grave's disease, myasthenia gravis, insulin resistance, and autoimmune hemolytic anemia. Diseases classified as probable include, to name a few, **rheumatoid arthritis**, scleroderma with anti-collagen antibodies (Abs), pernicious anemia, and some cases of diabetes mellitus.

SUMM [0572] The phrase "NF-.kappa.B inhibiting amount" means an amount of a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, sufficient to inhibit a NF-.kappa.B transcription factor in a particular animal or animal. . .

SUMM . . . case all stereoisomers thereof, both individual stereoisomers and mixtures of enantiomers or diastereomers, are included within the scope of the **sulfonylaminocarbonyl** derivatives useful in the present invention.

SUMM . . . in the present invention that contain a basic functional group are prepared by contacting the free base form of the **sulfonylaminocarbonyl** derivative with a sufficient amount of the desired acid, which amount is usually 1 molar equivalent, to produce the salt. . .

SUMM . . . in the present invention that contain an acidic functional group are prepared by contacting the free acid form of the **sulfonylaminocarbonyl** derivative with a sufficient amount of the desired base, which amount is usually 1 molar equivalent, to produce the salt. . .

SUMM [0580] Examples of **sulfonylaminocarbonyl** derivatives useful in the present invention are found below. The examples are for illustration purposes, and are not to be. . .

DETD [0831] **Sulfonylaminocarbonyl** derivatives useful in the present invention may be identified using the methods described below.

DETD . . . throughput screening assay that reliably identifies inhibitors of NF-.kappa.B mediated transcription. While the assay described below utilized inhibitors which were **sulfonylaminocarbonyl** derivatives useful in the present invention, the assay may be used to screen for any inhibitor of NF-.kappa.B mediated transcription.

DETD . . . wavelengths. Then the blue/green emission ratio was calculated. Percent inhibition was calculated by comparing fluorescence in the presence of a **sulfonylaminocarbonyl** derivative useful in the

present invention with fluorescence in the absence of said **sulfonylaminocarbonyl** derivative under conditions of maximum stimulation with TNF-.alpha. or IL-1.beta.. An IC.sub.50 for said **sulfonylaminocarbonyl** derivative was determined from a dose-response curve. This assay was designed to be optionally run in either high or low. . .

DETD . . . wells.

Column 2 G-H = MG, MG132 quality control.

Column 12 = B, Reagent background wells.

Columns 3-11 = O, **Sulfonylaminocarbonyl** derivatives in triplicate at a concentration of 10 .mu.M (for screening purposes) or at varying concentrations for dose response studies. . .

DETD [0869] b) Inhibitor: Added 10 .mu.L of a **sulfonylaminocarbonyl** derivative at 10.times. desired final concentration to the following wells: Added to all O wells (unknowns: cells, assay media, cytokine). . .

DETD [0871] d) Incubation after stimulation of cells with an activation cytokine, with or without a **sulfonylaminocarbonyl** derivative: 6 hours, 37.degree. C., 5% CO.sub.2 atmosphere

DETD [0878] Representative **sulfonylaminocarbonyl** derivatives useful in the present invention were tested at a concentration of 10 .mu.M for the ability to inhibit NF-.kappa.B. . .

DETD [0879] As shown by cell-based assay data, the **sulfonylaminocarbonyl** derivatives in Table 3 are inhibitors of NF-.kappa.B mediated transcription that are able to cross cell membranes and reach a target in a NF-.kappa.B signal pathway. Accordingly, the **sulfonylaminocarbonyl** derivatives are useful in the present invention for treating a disease or a disorder responsive to the inhibition of NF-.kappa.B such as, for example, **rheumatoid arthritis** and osteoarthritis, autoimmune diseases, psoriasis, asthma, cardiovascular diseases such as, for example, atherosclerosis, acute coronary syndromes including myocardial infarction and. . .

DETD . . . out the methods for treating a disease or a disorder responsive to the inhibition of NF-.kappa.B of the present invention, **sulfonylaminocarbonyl** derivatives useful in the present invention may be administered in a number of pharmaceutically acceptable oral and parenteral forms. Thus, the **sulfonylaminocarbonyl** derivatives can be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, or intraperitoneally. Also, the **sulfonylaminocarbonyl** derivatives can be administered by inhalation, for example, intranasally. Additionally, the **sulfonylaminocarbonyl** derivatives can be administered transdermally. The following dosage forms may comprise as the active component a compound of Formula I or Formula II, or another **sulfonylaminocarbonyl** derivative useful in the present invention, or a pharmaceutically acceptable salt thereof.

DETD [0893] Examples of pharmaceutical preparations of the **sulfonylaminocarbonyl** derivatives useful in the present invention are described below. Such preparations can be administered to a patient, including a human,. . .

CLM What is claimed is:

. . . a disorder responsive to inhibition of nuclear factor-.kappa.B (NF-.kappa.B) transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof.

2. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound of Formula I ##STR15## or a pharmaceutically acceptable salt thereof, wherein: X and Y are selected. . .

3. The method according to claim 2, wherein the **sulfonylaminocarbonyl** derivative is a compound of Formula I, or

a pharmaceutically acceptable salt thereof, selected from: (1,2,3,4-Tetrahydro-naphthalene-2-carbonyl)-sulfamic acid 2,6-diisopropyl-phenyl ester; [Bis-(4-chloro-phenyl)-acetyl]-sulfamic. . .

4. The method according to claim 2, wherein the **sulfonylaminocarbonyl** derivative is sulfamic acid [[2,4,6-tris(1-methylethyl)phenyl]acetyl]-2,6-bis(1-methylethyl)phenyl ester, or a pharmaceutically acceptable salt thereof.

5. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound of Formula II ##STR17## or a pharmaceutically acceptable salt thereof, wherein: R.sup.1 is hydrogen, alkyl, or. . .

6. The method according to claim 5, wherein the **sulfonylaminocarbonyl** derivative is a compound of Formula II, or a pharmaceutically acceptable salt thereof, selected from: 6-(3,5-Diisopropyl-4-{[(2,4,6-triisopropyl-phenyl)-acetyl]sulfamoyloxy}-phenyl)-hexanoic acid ethyl ester; 3-[3-(3,5-Diisopropyl-4-{[(2,4,6-triisopropyl-phenyl)-acetyl]sulfamoyloxy}-phenyl)-ureido]-propionic. . .

7. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound, or a pharmaceutically acceptable salt thereof, selected from: (9H-Xanthene-9-carbonyl)-sulfamic acid 2,6-diisopropyl-phenyl ester; ((E)-2-Methyl-3-phenyl-acryloyl)-sulfamic acid 2,6-diisopropyl-phenyl ester;. . .

8. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound, or a pharmaceutically acceptable salt thereof, selected from: Carbamic acid, [(phenylamino)sulfonyl]-, 2,6-bis(1-methylethyl)phenyl ester; Carbamic acid, [(phenylamino)sulfonyl]-,. . .

9. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound, or a pharmaceutically acceptable salt thereof, selected from: Urea, N-[2,6-bis(1-methylethyl)phenyl]-N'-[(dipropylamino)-sulfonyl]-; Urea, N-(2,2-dimethyl-4-phenyl-1,3-dioxan-5-yl)-N'-[[(tricyclo[3.3.1.1.sup.3,7]dec-1-ylmethyl)amino]sulfonyl]-, (4S-cis)-; Urea, N-(2,2-dimethyl4-phenyl-1,3-dioxan-5-yl)-N'-[[(2,2-dimethyl4-phenyl-1,3-dioxan-5-yl)amino]sulfonyl]-, stereoisomer;. . .

10. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound, or a pharmaceutically acceptable salt thereof, selected from: Sulfamic acid, [[[2,4,6-tris(1-methylethyl)phenyl]amino]-carbonyl]-, 2,6-bis(1-methylethyl)phenyl ester; Sulfamic acid, [[[[1-[4-(dimethylamino)phenyl]cyclopentyl]-methyl]amino]carbonyl],. . .

11. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound, or a pharmaceutically acceptable salt thereof, selected from: Carbamic acid, [(dodecyloxy)sulfonyl]-, dodecyl ester; Carbamic acid, [(dodecyloxy)sulfonyl]-,. . .

12. The method according to claim 1, wherein the **sulfonylaminocarbonyl** derivative is a compound, or a pharmaceutically acceptable salt thereof, selected from: N-[2,6-bis(1-methylethyl)phenyl]-N'-[(6-ethoxy-2-benzothiazolyl)-sulfonyl]-urea; N-[2,6-bis(1-methylethyl)phenyl]-N'-(2-octadecylsulfonyl)urea; N-[2,4,6-trimethoxyphenyl]-N'-(2-octadecylsulfonyl)urea; N-[2,6-bis(1-methylethyl)phenyl]-N'-(tetradecylsulfonyl)urea; N-[2,6-bis(1-methylethyl)phenyl]-N'-(dodecylsulfonyl)urea; N-[2,6-bis(1-methylethyl)phenyl]-N'-(hexadecylsulfonyl)urea; N-[2,6-bis(1-methylethyl)phenyl]-N'-methyl-N'-(dodecylsulfonyl)urea; N-[2,6-bis(1-methylethyl)phenyl]-N'-(tridecylsulfonyl)urea;. . .

. . . or a disorder responsive to inhibition of nuclear factor-.kappa.B transcription factors, comprising administering to a patient in need thereof a **sulfonylaminocarbonyl** derivative, or a pharmaceutically acceptable salt thereof, wherein the disease or disorder being treated is **rheumatoid arthritis**, osteoarthritis, an autoimmune disease, psoriasis, asthma, a cardiovascular disease, an acute coronary syndrome, congestive heart failure, Alzheimer's disease, multiple sclerosis,. . .
15. The method according to claim 13, wherein the disease or disorder being treated is **rheumatoid arthritis**.

30. A method of inhibiting NF-.kappa.B transcription factors in an animal, comprising administering to the animal a NF-.kappa.B inhibiting amount of a **sulfonylaminocarbonyl** derivative, or a pharmaceutical acceptable salt thereof.

L6 ANSWER 3 OF 25 USPATFULL on STN
AN 2002:323149 USPATFULL
TI Amino-substituted compounds useful as inhibitors of impdh enzyme
IN Iwanowicz, Edwin J., Cranbury, NJ, UNITED STATES
Leftheris, Katerina, Skillman, NJ, UNITED STATES
Liu, Chunjian, Lawrenceville, NJ, UNITED STATES
Mitt, Toomas, Plainsboro, NJ, UNITED STATES
Watterson, Scott H., Hamilton, NJ, UNITED STATES
PI US 2002183315 A1 20021205
AI US 2002-155274 A1 20020523 (10)
RLI Division of Ser. No. US 1999-428609, filed on 27 Oct 1999, GRANTED, Pat. No. US 6420403
PRAI US 1998-106184P 19981029 (60)
DT Utility
FS APPLICATION
LREP STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1760
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention discloses compounds useful in treating or preventing IMPDH-associated disorders, such as transplant rejection and autoimmune diseases, having the formula (I), ##STR1##

wherein X is --C(O)--, --C(S)--, or --S(O).sub.2--; A is an optionally-substituted saturated or unsaturated monocyclic or bicyclic ring; B is a saturated or unsaturated monocyclic or bicyclic ring system having at least one substituent Q which is selected from R.sup.7 and R.sup.8; R.sup.7 is selected from (C.sub.0-C.sub.6)alkyl, (C.sub.2-C.sub.6)alkenyl and (C.sub.2-C.sub.6)alkynyl and R.sup.7 is substituted with ##STR2##

R.sup.8 is selected from (C.sub.0-C.sub.6)alkyl, (C.sub.2-C.sub.6)alkenyl and (C.sub.2C.sub.6)alkynyl and R.sup.8 is substituted with ##STR3##

and Z.sup.1 through Z.sup.5 are as defined in the specification.
SUMM . . . MPA and derivatives of MPA, are useful drugs in the treatment of transplant rejection, autoimmune disorders, psoriasis, inflammatory diseases including **rheumatoid arthritis**, tumors, and allograft rejection. These are described in U.S. Pat. Nos. 4,686234, 4,725622, 4,727,069, 4,753,935, 4,786,637, 4,808,592, 4,861,776, 4,868,153, 4,948,793,. . .

SUMM . . . (C.sub.2-C.sub.6)alkenyl, (C.sub.2-C.sub.6)alkynyl, haloalkyl, haloalkoxy, OH, hydroxy(C.sub.1-C.sub.4)alkyl, (C.sub.1-C.sub.4)alkoxy, (C.sub.1-C.sub.4alkyl)carbonyl, NH.sub.2, (C.sub.1-C.sub.4alkyl).sub.1-2 alkylamino-, (C.sub.0-C.sub.4)alkylthio-, (C.sub.1-C.sub.4alkyl)sulfonyl-, aryl(C.sub.0-C.sub.4 alkyl)sulfonyl-, (C.sub.0-C.sub.4 alkyl).sub.0-2aminosulfonyl-, (C.sub.0-C.sub.4 alkyl)carbonylaminosulfonyl-, aryl(C.sub.0-C.sub.4 alkyl) **sulfonylaminocarbonyl**, (C.sub.1-C.sub.4alkyl) **sulfonylaminocarbonyl** carboxylate, (C.sub.1-C.sub.4)alkyloxycarbonyl, (C.sub.0-C.sub.4alkyl).sub.0-2aminocarbonyl-, and (C.sub.0-C.sub.4 alkyl)tetrazol-5-yl;

SUMM . . . CN, (C.sub.1-C.sub.4)alkyl, C.sub.3-C.sub.10 cycloalkyl, (C.sub.2-C.sub.6)alkenyl, (C.sub.2-C.sub.6)alkynyl, haloalkyl, haloalkoxy, OH, C.sub.1-C.sub.4alkoxy, C.sub.1-C.sub.4alkylcarbonyl, NH.sub.2, (C.sub.1-C.sub.4alkyl).sub.1-2alkylamino, CO--C.sub.4alkylthio, C.sub.1-C.sub.4 alkylsulfonyl, aryl(C.sub.0-C.sub.4alkyl)sulfonyl, (C.sub.0-C.sub.4alkyl).sub.0-2alkylaminosulfonyl-, (C.sub.0-C.sub.4 alkyl)carbonylaminosulfonyl-, aryl(C.sub.0-C.sub.4alkyl)**sulfonylaminocarbonyl**, (C.sub.1-C.sub.4alkyl) **sulfonylaminocarbonyl** carboxylate, C.sub.1-C.sub.4alkyloxycarbonyl, (C.sub.0-C.sub.4 alkyl).sub.0-2 aminocarbonyl-, and (C.sub.0-C.sub.4alkyl)tetrazol-5-yl; and

SUMM [0068] Examples of IMPDH-associated disorders include transplant rejection and autoimmune disorders, such as **rheumatoid arthritis**, multiple sclerosis, juvenile diabetes, asthma, and inflammatory bowel disease, as well as inflammatory disorders, cancer and tumor disorders, T-cell mediated. . .

SUMM . . . burn treatment), heart valve xenografts, serum sickness, and graft vs. host disease; in the treatment of autoimmune diseases, such as **rheumatoid arthritis**, psoriatic arthritis, multiple sclerosis, juvenile diabetes, asthma, inflammatory bowel disease (such as Crohn's disease and ulcerative colitus), pyoderma gangrenum, lupus. . .

SUMM . . . for the treatment of the aforementioned exemplary disorders irrespective of their etiology, for example, for the treatment of transplant rejection, **rheumatoid arthritis**, inflammatory bowel disease, and viral infections.

CLM What is claimed:

. . . (C.sub.2-C.sub.6)alkenyl, (C.sub.2-C.sub.6)alkynyl, haloalkyl, haloalkoxy, OH, hydroxy(C.sub.1-C.sub.4)alkyl, (C.sub.1-C.sub.4)alkoxy, (C.sub.1-C.sub.4alkyl)carbonyl, NH.sub.2, (C.sub.1-C.sub.4alkyl).sub.1-2 alkylamino-, (C.sub.0-C.sub.4)alkylthio-, (C.sub.1-C.sub.4alkyl)sulfonyl-, aryl(C.sub.0-C.sub.4 alkyl)sulfonyl-, (C.sub.0-C.sub.4 alkyl).sub.0-2aminosulfonyl-, (C.sub.0-C.sub.4 alkyl)carbonylaminosulfonyl-, aryl(C.sub.0-C.sub.4 alkyl) **sulfonylaminocarbonyl**, (C.sub.1-C.sub.4alkyl) **sulfonylaminocarbonyl** carboxylate, (C.sub.1-C.sub.4)alkyloxycarbonyl, (C.sub.0-C.sub.4alkyl).sub.0-2aminocarbonyl-, and (C.sub.0-C.sub.4 alkyl)tetrazol-5-yl; B is a saturated or unsaturated monocyclic or bicyclic ring system optionally comprising up. . . (C.sub.1-C.sub.4)alkyl, C.sub.3-C.sub.10 cycloalkyl, (C.sub.2-C.sub.6)alkenyl, (C.sub.2-C.sub.6)alkynyl, haloalkyl, haloalkoxy, OH, C.sub.1-C.sub.4alkoxy, C.sub.1-C.sub.4alkylcarbonyl, NH.sub.2, (C.sub.1-C.sub.4alkyl), .sub.2alkylamino, C.sub.0-C.sub.4alkylthio, C.sub.1-C.sub.4 alkylsulfonyl, aryl(C.sub.0-C.sub.4alkyl)sulfonyl, (C.sub.0-C.sub.4alkyl).sub.0.sub.2alkylaminosulfonyl-, (C.sub.0-C.sub.4 alkyl)carbonylaminosulfonyl-, aryl(C.sub.0-C.sub.4alkyl)**sulfonylaminocarbonyl**, (C.sub.1-C.sub.4alkyl)**sulfonylaminocarbonyl** carboxylate, C.sub.1-C.sub.4alkyloxycarbonyl, (C.sub.0-C.sub.4 alkyl).sub.0-2 aminocarbonyl-, and (C.sub.0-C.sub.4alkyl)tetrazol-5-yl; and R.sup.12 is selected from hydrogen, alkyl, (C.sub.1-C.sub.6)alkoxy,

C.sub.3-C.sub.6cycloalkyl, heterocycle and aryl.
18. The method of claim 15, wherein said IMPDH-associated disorder is selected from transplant rejection, **rheumatoid arthritis**, inflammatory bowel disease, hepatitis B, hepatitis C, herpes simplex I, and herpes simplex II.

L6 ANSWER 4 OF 25 USPATFULL on STN
AN 2002:61272 USPATFULL
TI Method for treating allergies
IN Gu, Yin, San Diego, CA, UNITED STATES
Karlsson, Lars, La Jolla, CA, UNITED STATES
Sun, Siquan, San Diego, CA, UNITED STATES
Thurmond, Robin L., San Diego, CA, UNITED STATES
PI US 2002035108 A1 20020321
US 6369032 B2 20020409
AI US 2001-946214 A1 20010905 (9)
PRAI US 2000-230407P 20000906 (60)
DT Utility
FS APPLICATION
LREP AUDLEY A. CIAMPORCERO JR., JOHNSON & JOHNSON, ONE JOHNSON & JOHNSON PLAZA, NEW BRUNSWICK, NJ, 08933-7003
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 2 Drawing Page(s)
LN.CNT 1336
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Use of cathepsin S inhibitors for the treatment of an allergic condition, in particular an atopic allergic condition, more specifically for the treatment of hay fever, asthma, atopic dermatitis or a food allergy.
SUMM . . . S are expected to find utility in the treatment of chronic autoimmune diseases including, but not limited to, lupus and **rheumatoid arthritis**; and have potential utility in modulating the immune response to tissue transplantation. Methods of modulating autoimmunity with an agent that. . .
CLM What is claimed is:
. . . Z is hydroxy, acyloxy, carboxyl, esterified carboxyl, amidated carboxyl, aminosulfonyl, (lower alkyl or aryl-lower alkyl)aminosulfonyl, or (lower alkyl or aryl-lower alkyl)**sulfonylaminocarbonyl**; or Z is tetrazolyl, triazolyl or imidazolyl; Q is direct bond, lower alkylene, Y.sub.1-lower alkylene or C.sub.2-C.sub.7-alkylene interrupted by Y.sub.1;. . .

L6 ANSWER 5 OF 25 USPATFULL on STN
AN 2002:45637 USPATFULL
TI Dipeptide nitriles
IN Altmann, Eva, Reinach, SWITZERLAND
Betschart, Claudia, Takarazuka, JAPAN
Gohda, Keigo, Hyogo, JAPAN
Horiuchi, Miyuki, Hyogo, JAPAN
Lattmann, Rene, Binningen, SWITZERLAND
Missbach, Martin, Gipf-Oberfrick, SWITZERLAND
Sakaki, Junichi, Hyogo, JAPAN
Takai, Michihiro, Ibaraki, JAPAN
Teno, Naoki, Hyogo, JAPAN
Cowen, Scott Douglas, Branchburg, NJ, United States
Greenspan, Paul David, New Providence, NJ, United States
McQuire, Leslie Wighton, Warren, NJ, United States
Tommasi, Ruben Alberto, Whitehouse Station, NJ, United States
van Duzer, John Henry, Asbury, NJ, United States
PA Novartis AG, Basel, SWITZERLAND (non-U.S. corporation)

PI US 6353017 B1 20020305
AI US 2000-643639 20000822 (9)
RLI Continuation of Ser. No. US 1998-186223, filed on 4 Nov 1998, now abandoned
PRAI GB 1997-23407 19971105
US 1997-108160P 19971205 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Gruenfeld, Norbert
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 3091
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB N-terminal substituted dipeptide nitriles as defined are useful as inhibitors of cysteine cathepsins, e.g. cathepsins B, K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions, including inflammation, **rheumatoid arthritis**, osteoarthritis, osteoporosis, tumors (especially tumor invasion and tumor metastasis), coronary disease, atherosclerosis (including atherosclerotic plaque rupture and destabilization). Particular dipeptide nitriles are compounds of formula I, or physiologically-acceptable and -cleavable esters or a salts thereof ##STR1##

wherein: the symbols are as defined.

In particular it has been found that by appropriate choice of groups R, R.sub.2, R.sub.3, R.sub.4, R.sub.5, X.sub.1, Y and L, the relative selectivity of the compounds as inhibitors of the various cysteine cathepsin types, e.g. cathepsins B, K, L and S may be altered, e.g. to obtain inhibitors which selectively inhibit a particular cathepsin type or combination of cathepsin types.

AB . . . K, L and S, and can be used for the treatment of cysteine cathepsin dependent diseases and conditions, including inflammation, **rheumatoid arthritis**, osteoarthritis, osteoporosis, tumors (especially tumor invasion and tumor metastasis), coronary disease, atherosclerosis (including atherosclerotic plaque rupture and destabilization). Particular dipeptide. . .

SUMM . . . cathepsins B, K, L and S, are a class of lysosomal enzymes which are implicated in various disorders including inflammation, **rheumatoid arthritis**, osteoarthritis, osteoporosis, tumors (especially tumor invasion and tumor metastasis), coronary disease, atherosclerosis (including atherosclerotic plaque rupture and destabilization), autoimmune diseases,. . .

SUMM Z is hydroxy, acyloxy, carboxyl, esterified carboxyl, amidated carboxyl, aminosulfonyl, (lower alkyl or aryl-lower alkyl)aminosulfonyl, or (lower alkyl or aryl-lower alkyl)**sulfonylaminocarbonyl**; or Z is tetrazolyl, triazolyl or imidazolyl;

SUMM . . . the Invention may be use for treatment or prophylaxis of diseases of excessive cartilage or matrix degradation, including osteoarthritis and **rheumatoid arthritis** as well as certain neoplastic diseases involving expression of high levels of proteolytic enzymes and matrix degradation.

SUMM The antiarthritic efficacy of the compounds of the invention for the treatment of **rheumatoid arthritis** can be determined using models such as or similar to the rat model of adjuvant arthritis, as described previously (R.. . .

SUMM . . . to mammals, including man, to inhibit cathepsin activity, and for the treatment of cathepsin dependent disorders, in particular inflammation, osteoporosis, **rheumatoid arthritis** and

osteoarthritis, and comprise an effective amount of a pharmacologically active compound of the invention, alone or in combination, with. . .

SUMM . . . treatment of cathepsin dependent conditions, such as cathepsin B, K, L and/or S dependent conditions, described herein, e.g. inflammation, osteoporosis, **rheumatoid arthritis** and osteoarthritis.

SUMM More specifically such relates to a method of treating **rheumatoid arthritis**, osteoarthritis, and inflammation (and other diseases as identified above) in mammals comprises administering to a mammal in need thereof a. . .

CLM What is claimed is:

. . . Z is hydroxy, acyloxy, carboxyl, esterified carboxyl, amidated carboxyl, aminosulfonyl, (lower alkyl or aryl-lower alkyl)aminosulfonyl, or (lower alkyl or aryl-lower alkyl)**sulfonylaminocarbonyl**; or Z is tetrazolyl, triazolyl or imidazolyl; Q is a direct bond, lower alkylene, Y.sub.1-lower alkylene or C.sub.2-C.sub.7-alkylene interrupted by. . .

. . . Z is hydroxy, acyloxy, carboxyl, esterified carboxyl, amidated carboxyl, aminosulfonyl, (lower alkyl or aryl-lower alkyl)aminosulfonyl, or (lower alkyl or aryl-lower alkyl)**sulfonylaminocarbonyl**; or Z is tetrazolyl, triazolyl or imidazolyl; Q is a direct bond, lower alkylene, Y.sub.1-lower alkylene or C.sub.2-C.sub.7-alkylene interrupted by. . .

. . . Z is hydroxy, acyloxy, carboxyl, esterified carboxyl, amidated carboxyl, aminosulfonyl, (lower alkyl or aryl-lower alkyl)aminosulfonyl, or (lower alkyl or aryl-lower alkyl)**sulfonylaminocarbonyl**; or Z is tetrazolyl, triazolyl or imidazolyl; Q is a direct bond, lower alkylene, Y.sub.1-lower alkylene or C.sub.2-C.sub.7-alkylene interrupted by. . .

. . . Z is hydroxy, acyloxy, carboxyl, esterified carboxyl, amidated carboxyl, aminosulfonyl, (lower alkyl or aryl-lower alkyl)aminosulfonyl, or (lower alkyl or aryl-lower alkyl)**sulfonylaminocarbonyl**; or Z is tetrazolyl, triazolyl or imidazolyl; Q is a direct bond, lower alkylene, Y.sub.1-lower alkylene or C.sub.2-C.sub.7-alkylene interrupted by. . .

20. A method according to claim 19 of treating inflammation, osteoporosis, **rheumatoid arthritis** and osteoarthritis.

L6 ANSWER 6 OF 25 USPATFULL on STN

AN 2001:4718 USPATFULL

TI Acylated enol derivative of .alpha.-ketoesters and .alpha.-ketoamides

IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., Plainfield, IN, United States
Mehdi, Shujaath, West Chester, OH, United States

PA Aventis Pharmaceuticals Inc., Bridgewater, NJ, United States (U.S. corporation)

PI US 6172044 B1 20010109

AI US 1999-303965 19990503 (9)

RLI Continuation of Ser. No. US 1997-978096, filed on 25 Nov 1997, now patented, Pat. No. US 5948886, issued on 7 Sep 1999 Continuation of Ser. No. US 1996-754081, filed on 20 Nov 1996, now abandoned

PRAI US 1995-31083P 19951201 (60)

DT Patent

FS Granted

EXNAM Primary Examiner: Jones, Dwayne C.; Assistant Examiner: Delacroix-Muirheid, C.

LREP Gupta, Balaram

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1633
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of .alpha.-ketoesters and .alpha.-ketoamides. The compounds of this invention are either prodrugs of known elastase inhibitors or are elastase inhibitors in their own right and are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema.

SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .

SUMM K is hydrogen, acetyl, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR2##

SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.

SUMM . . . In addition, amino protecting group K wherein K is acetyl, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, and 4-(**sulfonylaminocarbonyl**)phenylcarbonyl are described in European Patent Appl. Publ. No. 363 284, published Apr. 11, 1990 and U.S. Pat. No. 4,910,190, issued. . .

DETD a) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-COOH

DETD Scheme G, step a; Dissolve N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CO.sub.2 CH.sub.3 (677 mg, 1.0 mmol) in a THF:methanol:water (1:1:1) solvent mixture (30 mL) and treat with 1.0 N aqueous lithium. . .

DETD b) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro -Val-CONH.sub.2

DETD a) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CONHC.sub.6 H.sub.5

DETD . . . of formula I will be particularly useful include: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .

DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .

CLM What is claimed is:

. . . bVal, Pro or is deleted; K is hydrogen, acetyl, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**

)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR43## wherein Z is N or CH, B is a group of the. . .

. . . Nva, or Lys and K is hydrogen, acetyl, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)sulfonylamino(carbonyl)phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR45## wherein Z is N or CH, B is a group of the. . .

. . . Val, or Ala; P.sub.4 is Ala, Pro or is deleted; and K is acetyl, succinyl, t-butyloxycarbonyl, carbobenzyloxy, methoxysuccinyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR47## wherein Z is N or CH, B is a group of the. . .

. . . 4. A compound of claim 3 wherein R.sub.1 is isopropyl; P.sub.2 is Pro; and K is acetyl, t-butyloxycarbonyl, succinyl, methyoxysuccinyl, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, or is a group of the formula ##STR49## wherein Z is N or CH, B is a group of the. . .

L6 ANSWER 7 OF 25 USPATFULL on STN
AN 2000:9876 USPATFULL
TI Peptide, peptide analog and amino acid analog protease inhibitors
IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States
PA Sibia Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 6017887 20000125
AI US 1995-443931 19950518 (8)
RLI Continuation of Ser. No. US 1995-403420, filed on 13 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995, now patented, Pat. No. US 5804560
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Lukton, David
LREP Seidman, Stephanie L.Heller Ehrman White & McAuliffe
CLMN Number of Claims: 17
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3617
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or acetyl; Q is preferably --C(O)--; R.sub.B is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.
SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see,

e.g., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .

SUMM . . . alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); and (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl, and 4-[-(4-bromophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids. . .

L6 ANSWER 8 OF 25 USPATFULL on STN

AN 1999:170588 USPATFULL

TI Perfluoroalkyl ketone inhibitors of elastase and processes for making the same

IN Curran, Timothy T., Chester, NY, United States
Burkhart, Joseph P., Plainfield, IN, United States
Angelastro, Michael R., Mason, OH, United States
Peet, Norton P., Cincinnati, OH, United States
Metz, Jr., William A., Loveland, OH, United States

PA Hoechst Marion Roussel, Inc., Bridgewater, NJ, United States (U.S. corporation)

PI US 6008196 19991228
WO 9533762 19951214

AI US 1996-737905 19961122 (8)
WO 1995-US5363 19950501
19961122 PCT 371 date
19961122 PCT 102(e) date

RLI Continuation of Ser. No. US 1994-327520, filed on 20 Oct 1994, now patented, Pat. No. US 5403052 which is a continuation-in-part of Ser. No. US 1994-252857, filed on 2 Jun 1994, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Celsa, Bennett

LREP Gupta, Balaram

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1792

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to compounds which are inhibitors of elastase, particularly human neutrophil elastase, and to novel processes for making the same. As inhibitors of human neutrophil elastase, the compounds are useful in the treatment of a patient afflicted with a neutrophil associated inflammatory disease.

SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .

SUMM . . . useful as inhibitors of elastase. The compounds of formula I exhibit an anti-inflammatory effect useful in the treatment of gout, **rheumatoid arthritis** and other inflammatory diseases, such as adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, cystic fibrosis, chronic bronchitis, chronic obstructive. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

DETD . . . respiratory distress syndrome, septicemia, chronic bronchitis, inflammatory bowel disease (particularly ulcerative colitis or Crohn's disease), disseminated intravascular coagulation, gout and

rheumatoid arthritis. Compounds of formulae (I)-(IV) which are particularly preferred for the treatment of neutrophil associated inflammatory diseases include:

DETD . . . limited to emphysema, cystic fibrosis, adult respiratory distress syndrome, chronic bronchitis, inflammatory bowel disease, septicemia, disseminated intravascular coagulation, gout and **rheumatoid arthritis**. However, it is understood that the present invention is not limited by any particular theory or proposed mechanism to explain. . .

L6 ANSWER 9 OF 25 USPATFULL on STN
AN 1999:132782 USPATFULL
TI Acylated enol derivatives as prodrugs of elastase inhibitors
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., West Chester, OH, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Merrell Pharmaceuticals Inc., Bridgewater, NJ, United States (U.S. corporation)
PI US 5972897 19991026
AI US 1997-882764 19970626 (8)
RLI Division of Ser. No. US 1996-670136, filed on 25 Jun 1996, now patented, Pat. No. US 5698523, issued on 16 Dec 1997 which is a continuation of Ser. No. US 1995-420859, filed on 19 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-252798, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Stockton, Laura L.
LREP Gupta, Balaram
CLMN Number of Claims: 15
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1983
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of known elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema or as prodrugs of compounds which are useful in the treatment of said diseases.

SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .

SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.

DETD (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

DETD . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

DETD Preparation of (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide ##STR46## Method A; step a: N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[3,3,3-

trifluoro-1-(1-methylethyl)-2-oxopropyl]-L-prolinamide (54)
DETD To a stirred light suspension of 4-[(4-chlorophenyl) **sulfonylaminocarbonyl**]benzoic acid (0.68 g, 2.02 mmol; EP Pat. Appl. Publ. No. 0189305 B1) in CH.sub.2 Cl.sub.2 (18 mL) and DMF (2. . .
DETD (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide (MDL 105,928)
DETD . . . of formula I will be particularly useful nalude: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .
DETD (E)-N-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.
DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .
CLM What is claimed is:
9. A compound of claim 1 wherein said compound is (E)-N-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

L6 ANSWER 10 OF 25 USPATFULL on STN
AN 1999:128716 USPATFULL
TI Peptide, peptide analog and amino acid analog protease inhibitors
IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States
PA SIBIA Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 5969100 19991019
AI US 1995-403420 19950313 (8)
RLI Continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995, now patented, Pat. No. US 5804560
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia; Assistant Examiner: Lukton, David
LREP Seidman, Stephanie L.Heller Ehrman White & McAuliffe
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3687
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or acetyl; Q is preferably --C(O)--; R.sub.B is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.

SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e.g., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .

SUMM . . . (6) alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); and (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl carbonyl, and 4-[-(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids is. . .

L6 ANSWER 11 OF 25 USPATFULL on STN
AN 1999:106562 USPATFULL
TI Acylated enol derivatives of .alpha.-ketoesters and .alpha.-ketoamides
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., Plainfield, IN, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Hoechst Marion Roussel, Inc., Bridgewater, NJ, United States (U.S. corporation)
PI US 5948886 19990907
AI US 1997-978096 19971125 (8)
RLI Continuation of Ser. No. US 1996-754081, filed on 20 Nov 1996, now abandoned
PRAI US 1996-31083P 19961201 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delacroix-Muirheid, C.
LREP Gupta, Balaram
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1641
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of .alpha.-ketoesters and .alpha.-ketoamides. The compounds of this invention are either prodrugs of known elastase inhibitors or are elastase inhibitors in their own right and are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema.

SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .

SUMM K is hydrogen, acetyl, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenylcarbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR2## wherein Z is N or CH, B is a group of the. . .

SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.

SUMM . . . In addition, amino protecting group K wherein K is acetyl,

succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, and 4-(**sulfonylaminocarbonyl**)phenylcarbonyl are described in European Patent Appl. Publ. No. 363 284, published Apr. 11, 1990 and U.S. Pat. No. 4,910,190, issued. . .

DETD Preparation of L-Prolinamide, N-[4-[[[(4-chlorohenyl)sulfonyl]amino]carbonyl]benzoyl]-L-valyl-N-[2-(acetyloxy)-3-amino-1-(1-methylethyl)-3-oxo-1-propenyl]-, (E) ##STR25## a) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-COOH

DETD Scheme G, step a; Dissolve N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CO.sub.2 CH.sub.3 (677 mg, 1.0 mmol) in a THF:methanol:water (1:1:1) solvent mixture (30 mL) and treat with 1.0 N aqueous lithium. . .

DETD b) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CONH.sub.2

DETD Preparation of L-Prolinamide, N-[4-[[[(4-chlorophenyl)sulfonyl]amino]carbonyl]benzoyl]-L-valyl-N-[1-(1-methylethyl)-3-oxo-2-(acetyloxy)-3-(phenylamino)-1-propenyl]-, (E) ##STR26## a) Preparation of N-(4-((4-chlorophenyl)-**sulfonylaminocarbonyl**)phenylcarbonyl-Val-Pro-Val-CONHC.sub.6 H.sub.5

DETD . . . of formula I will be particularly useful include: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .

DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .

CLM What is claimed:

. . . bVal, Pro or is deleted; K is hydrogen, acetyl, succinyl, benzoyl, t-butyloxycarbonyl, carbobenzyloxy, dansyl, isovaleryl, methoxysuccinyl, 1-adamantanesulphonyl, 1-adamantaneacetyl, 2-carboxybenzoyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formulae ##STR43## wherein Z is N or CH, B is a group of the. . .

. . . Ile, Val, or Ala; P.sub.4 is Ala, Pro or is deleted; and K is acetyl, succinyl, t-butyloxycarbonyl, carbobenzyloxy, methoxysuccinyl, --C(O)N(CH.sub.3).sub.2, 4-((chlorophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-((4-bromophenyl)**sulfonylaminocarbonyl**)phenyl-carbonyl, 4-(**sulfonylaminocarbonyl**)phenylcarbonyl or is a group of the formula ##STR45## wherein Z is N or CH, B is a group of the. . .

. . . 3. A compound of claim 2 wherein R.sub.1 is isopropyl; P.sub.2 is Pro; and K is acetyl, t-butyloxycarbonyl, succinyl, methyoxysuccinyl, 4-((chlorophenyl)**sulfonylaminocarbonyl**)-phenylcarbonyl, or is a group of the formula ##STR47## wherein Z is N or CH, B is a group of the. . .

L6 ANSWER 12 OF 25 USPATFULL on STN
AN 1999:61253 USPATFULL
TI Peptide derivatives
IN Stein, Mark Morris, Wilmington, DE, United States
Trainor, Diane Amy, Glen Mills, PA, United States
PA Zeneca Inc., Wilmington, DE, United States (U.S. corporation)

PI US 5907068 19990525
AI US 1992-941001 19920904 (7)
RLI Division of Ser. No. US 1990-491757, filed on 9 Mar 1990, now patented, Pat. No. US 5194588 which is a division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Marshall, S. G.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5465
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.
SUMM . . . tools in pharmacological, diagnostic and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteo arthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives,. . .
SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .
SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .
SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .
SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .
SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and

sulfonylaminocarbonyl) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 1 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)**sulfonylaminocarbonyl**]ethyl;

SUMM . . . carboxy, methoxy, ethoxy, methoxycarbonyl, ethoxycarbonyl, methylcarbonylamino, an acylsulfonamido containing 2 carbons, (e.g., 4-(methylsulfonaminocarbonyl)phenyl), an acylsulfonamido containing 7 carbons (e.g., 4-(phenylsulfonylaminocarbonyl)phenyl, 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**)phenyl, or [(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl), an acylsulfonamido containing 11 carbons (e.g., 4(1-naphthylsulfonylaminocarbonylphenyl), an acylsulfonamido containing 14 carbons (e.g., 4-(4-bromophenylsulfonylamino(benzyl)carbonyl)phenyl); and an aryl group containing 6. . .

SUMM . . . ethenyl group substituted by a member selected from the group consisting of carboxy, ethoxycarbonyl, ureidocarbonyl (e.g., Z-2-(aminocarbonyl amino)ethenyl)), acylsulfonamidophenyl (e.g., 2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl]ethenyl), and 4-carboxyphenyl (e.g., E-2-(4-carboxyphenyl)ethenyl;

SUMM . . . to a warm-blooded animal in need thereof , particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit by. . .

DETD 3(RS)-4-I(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-NO.sub.2 .phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-f(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD b. 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br-.phi.)S(O.sub.2) NHC(O)].phi.,

R.sup.4 =H, A=CO, n=1).

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.4 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.-(CH.sub.2).sub.2, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenyl3-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =E-[4-[(4-Cl.phi.)S--(O.sub.2)NHC(O)].phi.--CH.dbd.CH--, R.sup.4 =H, A=CO, n=1)

DETD 3R(or S)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxo-pentyl))-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[4-(Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=OC, n=1)

DETD 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3R(or S)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenyl]carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD a. 1,1-Dimethylethyl 4-(4-chlorophenyl)**sulfonylaminocarbonyl**benzoate.

DETD b. 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzenecarboxylic acid.

DETD c. 2(RS),3(SR)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-2-hydroxy-4-methylpentyl)]-L-prolinamide (Formula VIIb, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4Cl-.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1).

DETD d. 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)--NHCO].phi., R.sup.4 =H, A=CO, n=1).

L6 ANSWER 13 OF 25 USPATFULL on STN

AN 1999:22082 USPATFULL

TI Methods of treating neurodegenerative disorders using protease inhibitors

IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States

Albrecht, Elisabeth, San Diego, CA, United States
PA Sibia Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 5872101 19990216
AI US 1995-444361 19950518 (8)
RLI Continuation of Ser. No. US 1995-403420, filed on 13 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Lukton, David
LREP Stephanie L. Seidman Heller Ehrman White & McAuliffe
CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3945
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 --(Q).sub.n is preferably benzyloxycarbonyl or acetyl; Q is preferably --C(O)--; R.sub.8 is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.
SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e.g., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .
SUMM . . . (6) alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl, and 4-[-(4-bromophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids. . .

L6 ANSWER 14 OF 25 USPATFULL on STN
AN 1999:12911 USPATFULL
TI Methods of treating neurodegenerative disorders using protease inhibitors
IN Munoz, Benito, San Diego, CA, United States
McDonald, Ian A., San Diego, CA, United States
Albrecht, Elisabeth, San Diego, CA, United States
PA Sibia Neurosciences, Inc., La Jolla, CA, United States (U.S. corporation)
PI US 5863902 19990126
AI US 1995-444912 19950518 (8)
RLI Continuation of Ser. No. US 1995-403420, filed on 13 Mar 1995 which is a continuation-in-part of Ser. No. US 1995-369422, filed on 6 Jan 1995
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Lukton, David
LREP Seidman, Stephanie L.Heller Erhman White & McAuliffe
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3888

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods of use of compounds and compounds for the treatment of disorders characterized by the cerebral deposition of amyloid are provided. Among the compounds are those of formulae (I), (II) and (III): ##STR1## in which R.sub.1 is preferably 2-methyl propene, 2-butene, norleucine; R.sub.2, R.sub.4, and R.sub.8 are each independently methyl or ethyl; R.sub.3 is preferably iso-butyl or phenyl; R.sub.5 is preferably iso-butyl; R.sub.6 is H or methyl; R.sub.7 -(Q).sub.n is preferably benzyloxycarbonyl or acetyl; Q is preferably --C(O)--; RB is preferbly iso-butyl; R.sub.A =--(T).sub.m --(D).sub.m --R.sub.1, is which T is preferably oxygen or carbon, and D is preferably a mono-unsaturated C.sub.3-4 alkenyl being more preferred; and X is an alcohol, particularly a secondary alcohol.

SUMM . . . a serine protease. This enzyme has been implicated as a pathogenic agent in a variety of disorders, including pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome (ARDS), glomerulonephritis and cystic fibrosis [see, e., Skiles et al. (1992) J. Med. Chem. 35:641-662; Angelastro. . .

SUMM . . . alkyl type protecting groups such as triphenylmethyl (trityl) and benzyl (Bn); and (7) trialkylsilane protecting groups such as trimethylsilane, 4-[-(4-chlorophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl, and 4-[-(4-bromophenyl) **sulfonylaminocarbonyl**] phenyl carbonyl. The preferred .alpha.-amino protecting group is t-butyloxycarbonyl (BOC); its use as an .alpha.-amino protecting group for amino acids. . .

L6 ANSWER 15 OF 25 USPATFULL on STN

AN 1998:25212 USPATFULL

TI Peptide derivatives

IN Edwards, Philip Duke, Claymont, DE, United States
Schwartz, John Anthony, Wilmington, DE, United States
Stein, Mark Morris, Wilmington, DE, United States
Trainor, Diane Amy, Glen Mills, PA, United States
Wildonger, Richard Alan, Newark, DE, United States

PA Zeneca Inc., Wilmington, DE, United States (U.S. corporation)

PI US 5726158 19980310

AI US 1995-467333 19950606 (8)

RLI Continuation of Ser. No. US 1990-482617, filed on 21 Feb 1990, now abandoned which is a division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned

PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122

DT Utility

FS Granted

EXNAM Primary Examiner: Johnson, Jerry D.

LREP Hohenschutz, Liza D.

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5961

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

SUMM . . . tools in pharmacological, diagnostic and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and

osteo arthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives,. .

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 1 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)

sulfonylaminocarbonyl]ethyl;

SUMM . . . carboxy, methoxy, ethoxy, methoxycarbonyl, ethoxycarbonyl, methylcarbonylamino, an acylsulfonamido containing 2 carbons, (e.g., 4-(methylsulfonaminocarbonyl)phenyl), an acylsulfonamido containing 7 carbons (e.g., 4-(phenylsulfonylaminocarbonyl)phenyl, 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl, or [(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl), an acylsulfonamido containing 11 carbons (e.g., 4(1-naphthylsulfonylaminocarbonylphenyl), an acylsulfonamido containing 14 carbons (e.g., 4-(4-bromophenylsulfonylamino(benzyl)carbonyl)phenyl); and an aryl group containing 6. . .

SUMM (X) an ethenyl group substituted by a member selected from the group consisting of carboxy, ethoxycarbonyl, ureidocarbonyl (e.g., Z-2-(aminocarbonylamino)ethenyl)), acylsulfonamidophenyl (e.g.,2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl]ethenyl), and 4-carboxyphenyl (e.g., E-2-(4-carboxyphenyl)ethenyl;

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, in particular for emphysema. The mode of administration may be oral; parenteral, including the subcutaneous deposit by. . .

DETD 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxo-pentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-NO.sub.2 .O slashed.)S(O.sub.2)NHCO].O slashed., R.sup.4 =H, A=CO, n=1)

DETD 3 (RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.O slashed.)S(O.sub.2)NHC(O)].O slashed., R.sup.4 =H, A=CO, n=1)

DETD b. 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br-.O slashed.)S(O.sub.2) NHC(O)].O slashed., R.sup.4 =H, A=CO, n=1).

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH, R.sup.3 =4-[(4-Cl.O slashed.)S(O.sub.2)NHC(O)].O slashed.--, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.O slashed.)S(O.sub.2)NHC(O)].O slashed.--(Ch.sub.2).sub.2, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =E-[4-[(4-Cl.O slashed.)S--(O.sub.2)NHC(O)].O slashed.--CH.dbd.CH--, R.sup.4 =H, A=CO, n=1)

DETD 3R(orS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxo-pentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[4-(Br.O slashed.)S(O.sub.2)NHC(O)].O slashed., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-

prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.O slashed.)S(O.sub.2)NHC(O)].O slashed., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.O slashed.)S(O.sub.2)NHC(O)].O slashed., R.sup.4 =H, A=CO, n=1)

DETD 3R(or S)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenyl]carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.O slashed.)S(O.sub.2)NHC(O)].O slashed., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.O slashed.)S(O.sub.2)NHCO].O slashed., R.sup.4 =H, A=CO, n=1)

DETD a. 1,1-Dimethylethyl 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate.

DETD b. 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzenecarboxylic acid.

DETD c. 2(RS),3(SR)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-2-hydroxy-4-methylpentyl)]-L-prolinamide (Formula VIIb, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4Cl-.O slashed.)S(O.sub.2)NHCO].O slashed., R.sup.4 =H, A=CO, n=1).

DETD d. 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.O slashed.)S(O.sub.2)--NHCO].O slashed., R.sup.4 =H, A=CO, n=1).

CLM What is claimed is:

. . . the aryl portion contains 6 carbons; (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)**sulfonylaminocarbonyl**]ethyl; (y) an alkyl group containing 2 or 10 carbons and substituted by methoxycarbonyl; (z) an alkyl group containing 2 to. . .

. . . 33) 3(RS)-N.sup.2 -(4-Hydroxycarbonylphenyl)aminocarbonyl-N.sup.6 -phenylmethoxycarbonyl-L-lysyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 34) 3(RS)-(4-Hydroxycarbonylphenyl)carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 35) 3(RS)-(Tricyclo[3.3.1.1.sup.3,7]dec-1-yl)sulfonyl-L-.alpha.-aminobutyryl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 36) 3(RS)-(4-Methoxycarbonylphenyl)carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 37) 3(RS)-(4-Hydroxycarbonylphenyl)aminocarbonyl-L-phenylalanyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 38) 3(RS)-(4-Methoxycarbonylphenyl)methoxycarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 39) 3(RS)-[E-3-(4-Ethoxycarbonylphenyl)-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 40) 3(RS)-(2-Ethoxycarbonylphenyl)aminocarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 41) 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 42) 3(RS)-Phenylmethoxycarbonyl-L-glutamyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide phenylmethyl ester; 43) 3S(or R)-(Tricyclo[3.3.1.1.sup.3,7]dec-1-yl)sulfonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 44) 3(RS)-

Phenylmethoxycarbonyl-L-[5-(phenylsulfonylamino)glutamyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 45) 3(RS)-[4-(Phenylsulfonylaminocarbonyl)phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 46) 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 47) 3(RS)-4-(1-Naphthylsulfonylamino)-1,4-dioxobutyl -L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 48) 3(RS)-[2-(4-Aminocarbonylphenoxy)-1-oxoethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 49) 3(RS)-(4-Hydroxycarbonylphenyl)methoxycarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 50) 3(RS)-[4-[4-(2-Amino-2-oxoethyl)phenoxy]-1-oxobutyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 51) 3(RS)-E-[3-(4-Hydroxycarbonylphenyl)-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 52) 3(RS)-[2-(4-Ethoxycarbonylphenoxy)-1-oxoethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 53) 3(RS)-[3-(4-Ethoxycarbonylphenyl)-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 54) 3(RS)-4-Hydroxybenzoyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 55) 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 56) 3(RS)-[3-(4-Hydroxycarbonylphenyl)-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 57) 3(RS)-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 58) 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 59) 3(RS)-[1-[4-[[(4-Bromophenyl)sulfonyl][phenylmethyl]aminocarbonyl]phenyl]-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 60) 3R(orS)-(Tricyclo[3.3.1.1.sup.3,7]dec-1-yl)sulfonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 61) 3S(orR)-[4-(Phenylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 62) 3S(or R)-Phenylmethoxycarbonyl-L-phenylglycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 63) 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 64) 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 65) 3S(or R)-Phenylmethoxycarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 66) 3S(or R)-[(4-Carboxyphenyl)aminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 67) 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 68) 3(RS)-N.sup.2,N.sup.6 -Di(phenylmethoxycarbonyl)-L-lysyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 69) 3(RS)-[1,4-Dioxo-4-(phenylsulfonylamino)butyl]-L-leucyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 70) 3(RS)-[4-(Methylsulfonylamino)-1,4-dioxobutyl]-L-leucyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 71) 3(RS)-N.sup.2 -[1,4-Dioxo-4-(phenylsulfonylamino)butyl]-N.sup.6 -phenylmethoxycarbonyl-L-lysyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; and 72) 3(RS)-[1,4-Dioxo-4-[(tricyclo[3.3.1.1.sup.3,7]dec-1-yl)sulfonylamino]butyl]-L-leucyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide.

. . . -[(phenylmethoxy)carbonyl]-L-lysyl-L-valyl-N-[3-(4-methyl-1,1,1-trifluoro-2-oxopentyl)]-L-prolinamide; 4) 3(RS)-[4-(Methylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-

trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 5) 3(RS)-[4-(Phenylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 6) 3(RS)-(4-Hydroxycarbonylphenyl)aminocarbonyl-L-.alpha.-aminobutyryl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 7) 3(RS)-[Z-(4-Aminocarbonylamino-1,4-dioxo-2-butenyl)]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 8) 3(RS)-[[4-[(1-Naphthylsulfonyl)aminocarbonyl]phenyl]aminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 9) 3(RS)-N.sup.2 -(4-Hydroxycarbonylphenyl)aminocarbonyl-N.sup.6 -phenylmethoxycarbonyl-L-lysyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 10) 3(RS)-(4-Hydroxycarbonylphenyl)carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 11) 3(RS)-(4-Hydroxycarbonylphenyl)aminocarbonyl-L-phenylalanyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 12) 3(RS)-4-[(4-Nitrophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 13) 3(RS)-Phenylmethoxycarbonyl-L-[5-(phenylsulfonylamino)glutamyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 14) 3(RS)-[4-(Phenylsulfonylaminocarbonyl)phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 15) 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 16) 3(RS)-4-(1-Naphthylsulfonylamino)-1,4-dioxobutyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 17) 3(RS)-(4-Hydroxycarbonylphenyl)methoxycarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 18) 3(RS)-E-[3-(4-Hydroxycarbonylphenyl)-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 19) 3(RS)-[4-[(4-Chlorophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 20) 3(RS)-[3-(4-Hydroxycarbonylphenyl)-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 21) 3(RS)-[3-[4-[(4-Chlorophenyl) **sulfonylaminocarbonyl**]phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 22) 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 23) 3S(orR)-[4-(Phenylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 24) 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 25) 3S(or R)-[4-[(4-Chlorophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 26) 3S(or R)-[(4-Carboxyphenyl)aminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 27) 3(RS)-[1,4-Dioxo-4-(phenylsulfonylamino)butyl]-L-leucyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; 28) 3(RS)-[4-(Methylsulfonylamino)-1,4-dioxobutyl]-L-leucyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; and 29) 3(RS)-N.sup.2 -[1,4-Dioxo-4-(phenylsulfonylamino)butyl]-N.sup.6 -phenylmethoxycarbonyl-L-lysyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide.

. . . method of treating a warm-blooded animal having a tissue degenerative disease selected from the group consisting of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, which method comprises administering to said animal a leukocyte elastase inhibiting effective amount of a compound of. . . .

. . . warm-blooded animal having a disease condition mediated by human leukocyte elastase selected from the group consisting of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, which method comprises administering to said animal a leukocyte elastase inhibiting effective amount of a compound of. . .

L6 ANSWER 16 OF 25 USPATFULL on STN
AN 97:118015 USPATFULL
TI Acylated enol derivatives as prodrugs of elastase inhibitors
IN Peet, Norton P., Cincinnati, OH, United States
Burkhart, Joseph P., West Chester, OH, United States
Mehdi, Shujaath, West Chester, OH, United States
PA Merrell Pharmaceuticals Inc., Cincinnati, OH, United States (U.S. corporation)
PI US 5698523 19971216
AI US 1996-670136 19960625 (8)
RLI Continuation of Ser. No. US 1995-420859, filed on 19 Apr 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-252798, filed on 2 Jun 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Stockton, Laura L.
LREP Boudreaux, William R.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 2060
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to acylated enol derivatives of known elastase inhibitors. These compounds are useful in the treatment of various inflammatory diseases, including cystic fibrosis and emphysema or as prodrugs of compounds which are useful in the treatment of said diseases.
SUMM . . . agent contributing to the tissue destruction associated with a number of inflammatory diseases such as chronic bronchitis, cystic fibrosis, and **rheumatoid arthritis**. J. L. Malech and J. I. Gallin, New Engl. J. Med., 317(11), 687 (1987). Elastase possesses a broad range of. . .
SUMM . . . an anti-inflammatory effect useful in the treatment of emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease; or are prodrugs of compounds which exhibit such effects.
DETD (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.
DETD . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolyl, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
DETD Preparation of (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide ##STR45##
DETD Method A; step a: N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[3,3,3-trifluoro-1-(1-methylethyl)-2-oxopropyl]-L-prolinamide (54)
DETD To a stirred light suspension of 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoic acid (0.68 g, 2.02 mmol; EP Pat. Appl. Publ. No. 0189305 B1) in CH.sub.2 Cl.sub.2 (18 mL) and DMF (2. . .
DETD Step b: (E)-N-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide (MDL 105,928)
DETD . . . of formula I will be particularly useful include: emphysema, cystic fibrosis, adult respiratory distress syndrome, septicemia,

disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. Compounds of formula I which are particularly preferred for the treatment of neutrophil associated. . .

DETD (E)-N-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoyl]-L-valyl-N-[2-(acetyloxy)-3,3,3-trifluoro-1-(1-methylethyl)-1-propenyl]-L-prolinamide.

DETD . . . for elastase-mediated diseases including but not limited to emphysema, cystic fibrosis, adult rspiratory distress syndrome, septicemia, disseminated intravascular coagulation, gout, **rheumatoid arthritis**, chronic bronchitis and inflammatory bowel disease. However, it is understood that the present invention is not limited by any particular. . .

L6 ANSWER 17 OF 25 USPATFULL on STN
AN 95:41068 USPATFULL
TI 1-alkyl-2-hydroxy-2-trifluoromethyl ethylamines
IN Stein, Mark M., Wilmington, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
PA Zeneca Inc., Wilmington, DE, United States (U.S. corporation)
PI US 5414132 19950509
AI US 1992-940932 19920904 (7)
RLI Division of Ser. No. US 1990-491757, filed on 9 Mar 1990, now patented, Pat. No. US 5194588 which is a division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.
LREP Cushman Darby & Cushman
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5536
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

SUMM . . . tools in pharmacological, diagnostic and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteo arthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives,. . .

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e.

acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 1 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)**sulfonylaminocarbonyl**]ethyl;

SUMM . . . carboxy, methoxy, ethoxy, methoxycarbonyl, ethoxycarbonyl, methylcarbonylamino, an acylsulfonamido containing 2 carbons, (e.g., 4-(methylsulfonaminocarbonyl)phenyl), an acylsulfonamido containing 7 carbons (e.g., 4-(phenylsulfonylaminocarbonyl)phenyl, 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl, or [(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl), an acylsulfonamido containing 11 carbons (e.g., 4(1-naphthylsulfonylaminocarbonylphenyl), an acylsulfonamido containing 14 carbons (e.g., 4-(4-bromophenylsulfonylamino(benzyl)carbonyl)phenyl); and an aryl group containing 6. . .

SUMM . . . an ethenyl group substituted by a member s elected from the group consisting of carboxy, ethoxycarbonyl, ureidocarbonyl (e.g., Z-2-(aminocarbonylamino)ethenyl)), acylsulfonamidophenyl

(e.g.,2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**
]phenyl]ethenyl), and 4-carboxyphenyl (e.g., E-2-(4-
carboxyphenyl)ethenyl;

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit by. . .

DETD 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-NO.sub.2 .phi.)S(O.sub.2)NHCO].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD b. 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-Br-.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH, R.sup.3 .dbd.4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--, R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3(RS)-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**
]phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.(CH.sub.2).sub.2, R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**
]phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.E-[4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--CH.dbd.CH--, R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3R(orS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxo-pentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3,R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[4-(Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3S (or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**
]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3R(or S)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**
]phenyl]carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.(CH.sub.3).sub.2 CH--, R.sup.3 .dbd.4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**

]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.3 .dbd.4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD a. 1,1-Dimethylethyl 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate

DETD b. 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzenecarboxylic acid

DETD c. 2(RS),3(SR)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-2-hydroxy-4-methylpentyl)]-L-prolinamide (Formula VIIb, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.3 .dbd.4-[(4Cl-.phi.)S(O.sub.2)NHCO].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

DETD d. 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 .dbd.CH(CH.sub.3)CH.sub.3, R.sup.2 .dbd.CH(CH.sub.3)CH.sub.3 , R.sup.3 .dbd.4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 .dbd.H, A.dbd.CO, n=1)

L6 ANSWER 18 OF 25 USPATFULL on STN

AN 93:63173 USPATFULL

TI Tetrahydroisoquinoline amides

IN Skiles, Jerry W., Brookfield, CT, United States

PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)

PI US 5232928 19930803

AI US 1991-792130 19911114 (7)

RLI Continuation of Ser. No. US 1990-536912, filed on 12 Jun 1990, now abandoned which is a continuation of Ser. No. US 1989-385140, filed on 25 Jul 1989, now abandoned

DT Utility

FS Granted

EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Turnipseed, James H.

LREP Frankhouser, D. E., Stempel, A. R., Timbers, M-E. M.

CLMN Number of Claims: 9

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 769

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Tetrahydroisoquinoline amides having the general structure ##STR1## are disclosed, the substituents defined hereinbelow, which amides are useful in inhibiting human leukocyte and neutrophil elastaes.

DETD . . . the treatment of tissue degenerative diseases. Additionally, such inhibitors could be used in the diagnosis and treatment of pulmonary emphysema, **rheumatoid arthritis**, osteoarthritis, and arteriosclerosis, among other diseases. The substituted amides of the present invention may be represented by the following formulae:. . .

DETD . . . of the present invention would be useful in the diagnosis and treatment of tissue degenerative diseases such as pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome - otherosclerosis, osteo arthritis, chronic obstructive lung disease, glomerular nephritis, inter alia.

DETD . . . be administered for the alleviation of conditions which include tissue degenerative diseases such as: pulmonary emphysema, artherosclerosis and osteo- and **rheumatoid arthritis**, in particular emphysema, and other diseases. The mode of administration may be parenteral, including the subcutaneous deposit of an osmotic. . .

DETD N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-

tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl-L-valyl]-(6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3'-(R,S)-[2'-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-leucyl]-spiro[cyclopentane-1,1'-(6.7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]]-carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-3-methyl -1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

DETD N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)]

DETD N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-carboxyl-pentyl)]

DETD 1,1-Dimethylethyl-4-](4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoate

DETD . . . over MgSO.sub.4 followed by filtration and evaporation a solid was obtaind which was treated with ether and filtered to yield 1,1-dimethylethyl-4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate (5.8 g, 42.3%) as a white solid (mp: above 300.degree. C.) which was used for hydrolysis.

DETD 4-](4-Chlorophenyl)**sulfonylaminocarbonyl**]benzene carboxylic acid

DETD . . . before being filtered, washed with water and dried to yield a white solid. Recrystallization from ethanol/water (1:1) gave the product 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**] benzene carboxylic acid in 63% yield melting at 285.degree.-287.degree. C.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]1,2,3,4-tetrahydro-3-isoquinolinecarboxamide

DETD . . . stated order in dry THF (35 mL) at 0.degree.-5.degree. C. L-Valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide (0.52 g, 1.21 mmol), HOBT (0.15 g, 1.1 mmol), 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzene carboxylic acid (0.37 g, 1.1 mmol), and WSCDI (0.45 g, 1.21 mmol). The mixture was stirred at 0.degree.-5.degree. C. for. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-1,2,3,4-tetrahydro-3-isoquinoline-carboxamide.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide (0.33 g, 0.44 mmol) was added to CH.sub.2 Cl.sub.2 (15mL) followed by Dess-Martin periodinane (0.56 g, 1.3 mmol) in CH.sub.2. . .

CLM What is claimed is:

3. A compound selected from the group consisting of:

N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy -1,2,3,4-tetrahydro-isoquinolyl)carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

N-[3-(R,S)-[2-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl-L-valyl]-(6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

N-[3-[2-[2-Amino-.alpha.-(methoxyimino)-4-thiazoleacetyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

N-[3-[2-[2-Amino-.alpha.-(carboxymethoxyimino)-4-

thiazolacetyl-L-valyl]-(5,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-Bromophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy -1,1-dimethyl-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3'-(R,S)-[2'-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-leucyl]-spiro [cyclopentane-1,1'-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]-carbonyl]-N-[3(1,1,1-trifluoro -4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-leucyl]-(1-benzyl -5,6,7-trimethoxy-1,2,3,4-tetrahydroisoquinolyl)]-carbonyl]-N-(3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3'-(R,S)-[2'-[2-Amino-.alpha.-(methoxyimino)-4-thiazolacetyl-L-valyl]-spiro[cyclohexane -1,1'-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl -2-oxopentyl)]amine N-[3'-(R,S)-[2'-[2-(methoxysuccinyl)amino-.alpha.-(methoxyimino)-4-thiazolacetyl-L-valyl(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-chlorophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-3-methyl -1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine N-[3-(R,S)-[2-[4-[(4-Bromophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(6,7-dimethoxy -1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)] N-[3-(R,S)-[2-[4-[(4-chlorophenyl) **sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl]-(1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1,-difluoro-2-oxo-4-methyl-1-carboxyl-pentyl)] N-[3'-(R,S)-[2'-[(2-methoxysuccinyl)amino-.alpha.-(methoxycarboxy)-4-thiazole-acetyl)-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N-[3-(1,1-difluoro-2-oxo-4-methyl-1-aminocarbonylpentyl)] N-[.alpha.-(methoxyimino)-2-furylacetyl-L-valyl]-(6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolyl)]carbonyl]-N -[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amine

L6 ANSWER 19 OF 25 USPATFULL on STN
AN 93:50536 USPATFULL
TI N-substituted amides
IN Skiles, Jerry W., Brookfield, CT, United States
PA Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, United States (U.S. corporation)
PI US 5221665 19930622
AI US 1991-686918 19910416 (7)
RLI Continuation of Ser. No. US 1989-426069, filed on 27 Oct 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Lester L.
LREP Frankhouser, D. E., Stempel, A. R., Timbers, M-E. M.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1435
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB N-substituted amides which inhibit hydrolysis of elastin, are described, which compounds are tri-and di- fluoromethyl ketone amide and non-naturally occurring n-substituted amino acids derivatives.
DETD . . . compounds may serve as diagnostic aids. Accordingly, such inhibitors could be used in the diagnosis and treatment of pulmonary emphysema, **rheumatoid arthritis**, osteoarthritis, and arteriosclerosis, among other diseases.
DETD . . . of the present invention would be useful in the diagnosis and

treatment of tissue degenerative diseases such as pulmonary emphysema, **rheumatoid arthritis**, adult respiratory distress syndrome, otherosclerosis, osteo arthritis, chronic obstructive lung disease, glomerular nephritis, inter alia.

DETD . . . be administered for the alleviation of conditions which include tissue degenerative diseases such as: pulmonary emphysema, arteriosclerosis and osteo- and **rheumatoid arthritis**, especially emphysema. The mode of administration may be parenteral, oral, intravenous, as a powder or liquid aerosol, or subcutaneous by. . .

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(n-hexyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(phenyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(4-trifluoromethylphenyl)glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(3,4-dimethoxyphenyl)glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-(N-methyl) valyl-N-(2,3-dihydro-1H-inden-1-yl) glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[2-(3-indolyl)ethyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-(N-cyclopentyl)valyl-N-(benzimidazo-2-yl) glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[(N-ethoxycarbonyl)piperidin-4-yl)]glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide [2-Amino-.alpha.-(methoxyimino)-4-thiazoleacetyl]-L-valyl-N-(2, 3-dihydro-1H-inden-5-yl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[1-[2-(morpholin-4-yl)]ethyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-leucyl-N-[1-[2-(pyrid-2-yl)]ethyl]-L-alanyl-N-[3-(1, 1,1-trifluoro-4-m ethyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(2-indanylmethyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(piperidin-1-yl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[1-[3-(pyrrolidin-2-one)-1-yl]propyl] glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Phenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl-L-valyl-N-[(tetrahydro-2H-pyran-2-yl)methyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-leucyl-N-(quinuclidin-3-yl)glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[(cyclohexyl)methyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[(2-pyrrole)methyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-

oxopentyl)]amide

DETD [[4-(Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(5,6-dimethoxy-2,3-dihydro-1H-inden-2-yl) glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-[L-2-oxohexamethyleneimine-3-yl)]glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(6,7,8,9-tetrahydro-5H-benzocyclohepten-7-yl) glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(5H-benzoimidazol-6-yl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]amide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(2,3-dihydro-1H-inden-2-yl)glycyl-N-[3-(1,1,1-trifluoro-4-(3,4-methylenedioxy) phenyl-2-oxobutyl)]amide

DETD [[4-(4-Bromophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl)]-L-valyl-N-(3-carboxypropyl)glycyl-N-[3-(1, 1,1-trifluoro-4-(3,4,5-trimethoxy)phenyl-2-oxobutyl)]amide

DETD 1,1-Dimethylethyl-4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**] benzoate

DETD . . . over MgSO.sub.4 followed by filtration and evaporation a solid was obtained which was treated with ether and filtered to yield 1,1-dimethylethyl-4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate (5.8 g, 42.3%) as a white solid (mp: above 300.degree. C.) which was used for hydrolysis. 4-[(4-Chlorophenyl) **sulfonylaminocarbonyl** benzene carboxylic acid

DETD . . . before being filtered, washed with water and dried to yield a white solid. Recrystallization from ethanol/water (1:1) gave the product 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**] benzene carboxylic acid in 63% yield melting at 285.degree.-287.degree. C.

DETD [4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-Valyl-N-2-(3,4-dimethoxy)phenethyl]-glycyl-N-3-(1, 1,1-trifluoro-4-methyl-2-hydroxypentyl)] amide

DETD . . . in dry THF (35 mL) at 0.degree.-5.degree. C.: L-Valyl-N-[2-(3,4-dimethoxy)phenethyl]glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-hydroxypentyl]amide (0.8 g, 1.63 mmol), hydroxybenzotriazole (HOBT), 0.2 g, 1.48 mmol), 4-[(4-chlorophenyl)-**sulfonylaminocarbonyl**]benzene carboxylic acid (0.5 g, 1.48 mmol), WSCDI (0.312 g, 1.63 mmol) and triethylamine (0.165 g, 1.63 mmol). The mixture was. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-Valyl-N-[2-(3,4-dimethoxy)phenethyl] glycyl-N-[3-(1,1,1-trifluoro-4-methyl- 2-hydroxypentyl)] amide (0.4 g, 0.492 mmol) was added to THF (20 mL) followed by Dess-Martin periodinane (0.42 g,. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl 1-L-Valyl-N-(2-indanyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]amide

DETD . . . following reactants were mixed in the stated order in L-valyl-N-(2-indanyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]amide (1.3 g, 2.93 mmol), hydroxybenzotriazole (HOBT), (0.36 g, 2.66 mmol), 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzene carboxylic acid (0.9 g, 2.64 mmol) and WSCDI (0.56 g, 2.92 mmol). The mixture was stirred at 0.degree.-5.degree. C. for. . .

DETD [4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-valyl-N-(2-indanyl)glycyl-N-3-(1,1,1-trifluoro-4-methyl-2-oxypentyl)lamide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(2-indanyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)]amide (1.6 g, 2.1 mmol) was added to THF (25 mL) followed by Dess-Martin periodinane (2.66 g, 6.3 mmol). . .

DETD [4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl

-L-Valyl-N-(exo-bicyclo2. 2.1]hept-2-yl) glycyl-N-3-(1,1,1-trifluoro-4-methyl-2-hydroxy-pentyl)]amide.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-Valyl-N-(exo-bicyclo[2,2,1]hept-2-yl)-glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-oxypentyl)] amide.

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-valyl-N-(exo-bicyclo[2.2.1]hept-2-yl)-glycyl-N-[3-(1, 1,1-trifluoro-4-methyl-2-hydroxy-pentyl)]amide (0.6 g, 0.807 mmol) was added to CH.sub.2 Cl.sub.2 (20 mL) followed by Dess-Martin periodinane (0.69 g,. . .

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-Valyl-N-(cyclopentyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxypentyl)amide]

DETD (4-(4-Chlorophenyl)**sulfonylaminocarbonyl** phenyl-1-oxomethyl]-L-Valyl-N-cyclopentyl-glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxypentyl)lamide

DETD [[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl-1-oxomethyl]-L-Valyl-N-(cyclopentyl)glycyl-N-[3-(1,1,1-trifluoro-4-methyl-2-hydroxy pentyl)]amide (0.72 g, 1.0 mmol) was added to THF (20 mL) followed by Dess-Martin periodinane (1.27 g, 3.0 mmol). . .

L6 ANSWER 20 OF 25 USPATFULL on STN

AN 93:20683 USPATFULL

TI Aminoalcohol intermediates for peptide derivatives

IN Edwards, Philip D., Claymont, DE, United States
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Stein, Mark M., Wilmington, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
Wildonger, Richard A., Newark, DE, United States

PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)

PI US 5194588 19930316

AI US 1990-491757 19900309 (7)

RLI Division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned

PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122

DT Utility

FS Granted

EXNAM Primary Examiner: Lee, Lester L.

LREP Miano, Rosemary M., Jackson, Thomas E.

CLMN Number of Claims: 7

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5515

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

SUMM . . . tools in pharmacological, diagnostic and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteo arthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives,. .
.

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it

is the terminal. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 1 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)**sulfonylaminocarbonyl**]ethyl;

SUMM . . . carboxy, methoxy, ethoxy, methoxycarbonyl, ethoxycarbonyl, methylcarbonylamino, an acylsulfonamido containing 2 carbons, (e.g., 4-(methylsulfonaminocarbonyl)phenyl), an acylsulfonamido containing 7 carbons (e.g., 4-(phenylsulfonylaminocarbonyl)phenyl, 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl, or

[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl), an acylsulfonamido containing 11 carbons (e.g., 4(1-naphthylsulfonylaminocarbonylphenyl), an acylsulfonamido containing 14 carbons (e.g., 4-(4-bromophenylsulfonylamino(benzyl)carbonyl)phenyl); and an aryl group containing 6. . .

SUMM . . . an ethenyl group substituted by a member selected from the group consisting of carboxy, ethoxycarbonyl, ureidocarbonyl (e.g., Z-2-(aminocarbonylamino)ethenyl)), acylsulfonamidophenyl (e.g., 2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-ethenyl), and 4-carboxyphenyl (e.g., E-2-(4-carboxyphenyl)ethenyl;

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit by. . .

DETD 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-NO.sub.2 .phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=Co, n=1)

DETD 3(RS)-[4-[4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.2 =H, A=CO, n=1)

DETD b. 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br-.phi.)S(O.sub.2) NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopenyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[3-[4-(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.(CH.sub.2).sub.2, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopenyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =E-[4-[4-(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--CH.dbd.CH--, R.sup.4 =H, A=CO, n=1)

DETD 3R(orS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxo-pentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[4-(Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3R(or S)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**

]-phenyl]carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD a. 1,1-Dimethylethyl 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate

DETD b. 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzenecarboxylic acid

DETD c. 2(RS),3(SR)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-2-hydroxy-4-methylpentyl)]-L-prolinamide (Formula VIIb, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4Cl-.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD d. 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(3-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

CLM What is claimed is:

. . . to 13 carbons; (w) arylsulfonamido wherein the aryl group contains 6, 10 or 12 carbons; (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal portion of the acylsulfonamide. . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

. . . to 13 carbons; (w) arylsulfonamido wherein the aryl group contains 6, 10 or 12 carbons; (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal portion of the acylsulfonamide. . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

L6 ANSWER 21 OF 25 USPATFULL on STN

AN 91:82198 USPATFULL

TI Peptide derivatives

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PI US 5055450 19911008

AI US 1990-493025 19900313 (7)

RLI Division of Ser. No. US 1987-5538, filed on 20 Jan 1987, now patented, Pat. No. US 4910190 which is a continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned

PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-5124 19850122

DT Utility

FS Granted

EXNAM Primary Examiner: Lee, Lester L.; Assistant Examiner: Davenport, Avis
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6077
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.
SUMM . . . tools in pharmacological, diagnostic and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteo arthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives,. .
.
SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .
SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .
SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .
SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .
SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .
SUMM . . . 6 carbons), alkoxy carbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .
SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .
SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e.,

acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 1 to 15 carbons (e.g., 4-[(4-chlorophenyl) -**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(I -adamantyl) **sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl) **sulfonylaminocarbonyl**]ethyl;

SUMM . . . carboxy, methoxy, ethoxy, methoxycarbonyl, ethoxycarbonyl, methylcarbonylamino, an acylsulfonamido containing 2 carbons, (e.g., 4-(methylsulfonaminocarbonyl)phenyl), an acylsulfonamido containing 7 carbons (e.g., 4-(phenylsulfonylaminocarbonyl)phenyl, 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl, or [(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl), an acylsulfonamido containing 11 carbons (e.g., 4(1-naphthylsulfonylaminocarbonylphenyl), an acylsulfonamido containing 14 carbons (e.g., 4-(4-bromophenylsulfonylamino(benzyl)carbonyl)phenyl); and an aryl group containing 6. . .

SUMM (X) an ethenyl group substituted by a member selected from the group consisting of carboxy, ethoxycarbonyl, ureidocarbonyl (e.g., Z-2-(aminocarbonylamino)ethenyl)), acylsulfonamidophenyl (e.g.,2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-ethenyl), and 4-carboxyphenyl (e.g., E-2-(4-carboxyphenyl)ethenyl;

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit by. . .

DETD 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-NO.sub.2 .phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD b. 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br-.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1).

DETD 3(RS)-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.(CH.sub.2).sub.2, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3,

R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =E-[4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--CH.dbd.CH--, R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3R(or S)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 H, A=CO, n=1)

DETD a. 1,1-Dimethylethyl 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate.

DETD b. 4-[4-Chlorophenyl)**sulfonylaminocarbonyl**]benzenecarboxylic acid.

DETD c. 2(RS),3(SR)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-2-hydroxy-4-methylpentyl)]-L-prolinamide

DETD d. 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1).

CLM What is claimed is:

. . . to 13 carbons; (w) arylsulfonamido wherein the aryl group contains 6, 10 or 12 carbons; (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal portion of the acylsulfonamide. . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . . by a member selected from carboxy, alkxoycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . . to 13 carbons; (w) arylsulfonamido wherein the aryl group contains 6, 10 or 12 carbons; (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazol, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 5 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acrylsulfonamido contains an aryl the aryl may be further

substituted by. . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acrylsulfonamido contains an aryl the aryl may be further. . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

. . . the aryl portion contains 6 carbons; (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl), 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)**sulfonylaminocarbonyl**]ethyl; (y) an alkyl group containing 2 or 10 carbons and substituted by methoxycarbonyl; (z) an alkyl group containing 2 to. . .

. . . to 13 carbons; (w) arylsulfonamido wherein the aryl group contains 6, 10 or 12 carbons; (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal portion of the acylsulfonamide. . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl may be further substituted by a member. . .

7. A compound of formula VIIb ##STR10## wherein: R.sup.1 is isopropyl; R.sup.2 is isopropyl; R.sup.3 is 4-[1-naphthylsulfonyl)aminocarbonyl]phenyl, 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl, or 4-[4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl; R.sup.4 is hydrogen; n=1; and A is ##STR11## or a base addition salt thereof.

L6 ANSWER 22 OF 25 USPATFULL on STN
AN 90:36303 USPATFULL
TI Difluoro keto compounds and their use as HLE inhibitors
IN Trainor, Diane A., Glen Mills, PA, United States
Stein, Mark M., Wilmington, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4923890 19900508
AI US 1987-51951 19870519 (7)
RLI Continuation-in-part of Ser. No. US 1987-3993, filed on 16 Jan 1987, now abandoned
PRAI GB 1986-13704 19860605
DT Utility
FS Granted
EXNAM Primary Examiner: Lee, Mary C.; Assistant Examiner: Richter, J.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1,10
DRWN No Drawings
LN.CNT 2394
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to selected difluoro compounds of formulae Ia, Ib and Ic (set out hereinafter) which are useful as inhibitors of human leukocyte elastase.
SUMM . . . research tools in pharmacological and related studies and in

the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteoarthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives, processes. . .

SUMM (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkanoyloxy (2 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 2 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10. . .

SUMM . . . group consisting of carboxy, alkoxycarbonyl wherein the alkoxy group contains 1 to 4 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkanoyloxy (2 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy,

aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . group consisting of carboxy, alkoxycarbonyl wherein the alkoxy group contains 1 to 4 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 2 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, but in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit. . .

L6 ANSWER 23 OF 25 USPATFULL on STN
AN 90:21543 USPATFULL
TI Peptide derivatives
IN Bergeson, Scott H., Wilmington, DE, United States
Edwards, Philip D., Claymont, DE, United States
Schwartz, John A., Wilmington, DE, United States
Shaw, Andrew, Kennett Square, PA, United States
Stein, Mark M., Wilmington, DE, United States
Trainor, Diane A., Glen Mills, PA, United States
Wildonger, Richard A., Newark, DE, United States
Wolanin, Donald J., Wilmington, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4910190 19900320
AI US 1987-5538 19870120 (7)
RLI Continuation-in-part of Ser. No. US 1986-821150, filed on 21 Jan 1986, now abandoned
PRAI GB 1985-1522 19850122
GB 1985-1523 19850122
GB 1985-1524 19850122

DT Utility
FS Granted
EXNAM Primary Examiner: Phillips, Delbert R.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 5524
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns pharmaceutically useful trifluoromethyl ketone substituted di-, tri- and tetra-peptide derivatives of the formulae Ia, Ib, Ic set out hereinafter, and salts thereof, which are inhibitors of human leukocyte elastase. Also described herein are pharmaceutical compositions containing a peptide derivative and processes and intermediates for use in the manufacture of the peptide derivatives.

SUMM . . . tools in pharmacological, diagnostic and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteo arthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives,. . .

DETD (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

DETD . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

DETD . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

DETD . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 1 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted. . .

DETD (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

DETD . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

DETD . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

DETD . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

DETD . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

DETD . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

DETD . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 1 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

DETD (x) ethyl substituted by an acylsulfonamido selected from the group consisting of 2-(methylsulfonylaminocarbonyl)ethyl, 2-(phenylsulfonylaminocarbonyl)ethyl, 2-[(1-adamantyl)**sulfonylaminocarbonyl**]ethyl, and 2-[(1-naphthyl)**sulfonylaminocarbonyl**]ethyl;

DETD . . . carboxy, methoxy, ethoxy, methoxycarbonyl, ethoxycarbonyl, methylcarbonylamino, an acylsulfonamido containing 2 carbons, (e.g., 4-(methylsulfonaminocarbonyl)phenyl), an acylsulfonamido containing 7 carbons (e.g., 4-(phenylsulfonylaminocarbonyl)phenyl, 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl, or [(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl), an acylsulfonamido containing 11 carbons (e.g., 4(1-naphthylsulfonylaminocarbonylphenyl), an acylsulfonamido containing 14 carbons (e.g., 4-(4-bromophenylsulfonylamino(benzyl)carbonyl)phenyl); and an aryl group containing 6. . .

DETD . . . an ethenyl group substituted by a member selected from the group consisting of carboxy, ethoxycarbonyl, ureidocarbonyl (e.g., Z-2-(aminocarbonylamino)ethenyl)), acylsulfonamidophenyl (e.g., 2-[4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl]ethenyl), and 4-carboxyphenyl (e.g., E-2-(4-carboxyphenyl)ethenyl;

DETD . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit by. . .

DETD 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH-, R.sup.3 =4-[(4-NO.sub.2 .phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH-, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD b. 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]-phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH-, R.sup.3 =4-[(4-Br-.phi.)S(O.sub.2) NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.--, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxopropyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-

oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi.(CH.sub.2).sub.2, R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-E-[3-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]-1-oxoprop-2-enyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =E-[4-[(4-Cl.phi.)S-(O.sub.2)NHC(O)].phi.-CH=CH--, R.sup.4 =H, A=CO, n=1)

DETD 3R(orS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxo-pentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[4-(Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Br.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3R(or S)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenyl]carbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =(CH.sub.3).sub.2 CH--, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHC(O)].phi., R.sup.4 =H, A=CO, n=1)

DETD 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD a. 1,1-Dimethylethyl 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate

DETD b. 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzenecarboxylic acid

DETD c. 2(RS),3(SR)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-2-hydroxy-4-methylpentyl)]-L-prolinamide (Formula VIIb, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4Cl-.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

DETD d. 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide (Formula Ib, R.sup.1 =CH(CH.sub.3)CH.sub.3, R.sup.2 =CH(CH.sub.3)CH.sub.3, R.sup.3 =4-[(4-Cl.phi.)S(O.sub.2)NHCO].phi., R.sup.4 =H, A=CO, n=1)

CLM What is claimed is:

. . . to 13 carbons; (w) arylsulfonamido wherein the aryl group contains 6, 10 or 12 carbons; (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal portion of the acylsulfonamide. . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (1 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . . . 12 carbons; R.sup.3 is an aryl group containing 6, 10 or 12 carbons suitably substituted by acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 1 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl may be further. . .

. . . A compound as claimed in claim 1 selected from the group consisting of: (a) 3(RS)-[4-(Methylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (b) 3(RS)-[4-(Phenylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (c) 3(RS)-[[4-[(1-Naphthylsulfonyl)aminocarbonyl]phenyl]aminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (d) 3(RS)-4-[(4-Nitrophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (e) 3(RS)-[4-(Phenylsulfonylaminocarbonyl)phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (f) 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (g) 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (h) 3S(or R)-[4-(Phenylsulfonylaminocarbonyl)phenylaminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (i) 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; and (j) 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide.

5. A compound as claimed in claim 5 selected from the group consisting of: (1) 3(RS)-[[4-[(1-Naphthylsulfonyl)aminocarbonyl]phenyl]aminocarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (2) 3(RS)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (3) 3(RS)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; (4) 3S(or R)-[4-[(4-Bromophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide; and (5) 3S(or R)-[4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]phenylcarbonyl]-L-valyl-N-[3-(1,1,1-trifluoro-4-methyl-2-oxopentyl)]-L-prolinamide.

L6 ANSWER 24 OF 25 USPATFULL on STN
AN 89:92486 USPATFULL
TI Selected difluoro derivatives
IN Trainor, Diane A., Glen Mills, PA, United States
Stein, Mark M., Wilmington, DE, United States
PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)
PI US 4880780 19891114
AI US 1987-58079 19870604 (7)
RLI Continuation-in-part of Ser. No. US 1986-872106, filed on 6 Jun 1986, now abandoned
PRAI GB 1985-14436 19850607
GB 1985-14438 19850607
GB 1985-14440 19850607
DT Utility
FS Granted
EXNAM Primary Examiner: Phillips, Delbert R.
LREP Miano, Rosemary M., Jackson, Thomas E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2503
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention discloses a series of difluoroketone, mono- di- and

tri-peptide derivatives of formula Ia, Ib and Ic:

(Formula set out on pages following Examples)
Ia
(Formula set out on pages following Examples)
Ib
(Formula set out on pages following Examples)
Ic

and salts thereof where appropriate, and wherein the radicals are defined hereafter in the specification. The derivatives are useful in inhibiting the action of human leukocyte elastase. There are also disclosed methods and intermediates for the manufacture of, and pharmaceutical compositions comprising, the said derivatives.

SUMM . . . research tools in pharmacological and related studies and in the treatment of tissue degenerative diseases such as pulmonary emphysema, atherosclerosis, **rheumatoid arthritis** and osteoarthritis in warm blooded animals. The invention also includes intermediates useful in the synthesis of these peptide derivatives, processes. . .

SUMM (x) acylsulfonamideo (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkylcarbonyloxy (2 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM (x) acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. .

SUMM . . . (2 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e., acylaminosulfonyland **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including

acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 2 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10. . .

SUMM . . . group consisting of carboxy, alkoxycarbonyl wherein the alkoxy group contains 1 to 4 carbons, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkanoyloxy (2 to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . to 6 carbons), alkoxy (1 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsulfonamido (i.e., acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl may be further substituted by. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 2 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, but in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit. . .

DETD c. 1,1-Dimethylethyl 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]benzoate

DETD d. 4-[(4-Chlorophenyl)**sulfonylaminocarbonyl**]benzoic acid

L6 ANSWER 25 OF 25 USPATFULL on STN

AN 89:84234 USPATFULL

TI Difluoro peptide compounds

IN Trainor, Diane A., Glen Mills, PA, United States

PA ICI Americas Inc., Wilmington, DE, United States (U.S. corporation)

PI US 4873221 19891010

AI US 1987-51952 19870519 (7)

PRAI GB 1986-13703 19860605

DT Utility

FS Granted

EXNAM Primary Examiner: Phillips, Delbert R.

LREP Miano, Rosemary M., Jackson, Thomas E.

CLMN Number of Claims: 4

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1691

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to selected difluoro compounds of formulae Ia, Ib and Ic (set out hereinafter) which are useful as inhibitors of human leukocyte elastase.

SUMM (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkanoyloxy (2 to 6 carbons), alkoxycarbonyl (1 to 6 carbons), carboxy, 5-tetrazolo, and acylsufonamido (i.e.

acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . by a member selected from carboxy, alkoxycarbonyl, where alkoxy is 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM . . . a member selected from carboxy, alkoxycarbonyl, where the alkoxy has 1 to 3 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing 2 to 15 carbons and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or. . .

SUMM (x) acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons), and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . to 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonylamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . 6 carbons), alkoxycarbonyl (2 to 6 carbons), carboxy, aminocarbonylalkyl (2 to 6 carbons), aminocarbonyl, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons, carboxy, alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) containing from 2 to 15 carbons, and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10. . .

SUMM . . . group consisting of carboxy, alkoxycarbonyl wherein the alkoxy group contains 1 to 4 carbons, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) including acylsulfonamido wherein the acyl group contains 1 to 7 carbons when it is the terminal. . .

SUMM . . . to 6 carbons), alkanoyloxy (2 to 6 carbons), alkoxycarbonyl (2 to 6 carbons) carboxy, 5-tetrazolo, and acylsulfonamido (i.e. acylaminosulfonyl and **sulfonylaminocarbonyl**) (2 to 15 carbons) and provided that when the acylsulfonamido contains an aryl the aryl contains 6, 10 or 12. . .

SUMM . . . alkylcarbonylamino wherein the alkyl group contains 1 to 6 carbons, 5-tetrazolo, and acylsulfonamido containing from 2 to 15 carbons (e.g., 4-[(4-chlorophenyl)**sulfonylaminocarbonyl**]phenyl or 4-[(4-bromophenyl)**sulfonylaminocarbonyl**]phenyl);

SUMM . . . administered to a warm-blooded animal in need thereof, particularly a human, for the treatment of conditions of pulmonary emphysema, atherosclerosis, **rheumatoid arthritis**, and osteo arthritis, but in particular for emphysema. The mode of administration may be oral, parenteral, including the subcutaneous deposit. . .